Université de Montréal

# Réorganisation cérébrale et surdité : Exploration des réseaux fonctionnels au repos

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*Ce mémoire intitulé*

# Réorganisation cérébrale et surdité : Exploration des réseaux fonctionnels au repos

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*A été évalué par un jury composé des personnes suivantes*
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# Résumé

L'activité neuronale partagée entre les différentes régions cérébrales permet d'estimer les patrons d'activation fonctionnelle à l'échelle de réseaux distribués, même en l'absence de paradigme. Constamment rapportés dans la population saine, les réseaux fonctionnels au repos (RSNs) peuvent être utilisés comme objet d'étude pour comprendre la contribution du développement sensoriel atypique sur la communication globale inter-réseau. À ce jour, peu d'études ont exploré l'organisation cérébrale au repos dans le contexte de la surdité. Pourtant, de multiples évidences soutiennent l'importance des entrées sensorielles en début de vie dans la consolidation de l'architecture fonctionnelle du cerveau. L'étude présentée dans ce mémoire a été développée et conceptualisée pour rendre compte de la relation entre la privation sensorielle et l'activité cérébrale spontanée entre les RSNs. À cette fin, 17 personnes avec une surdité congénitale de degré sévère à profond et 18 personnes entendantes non signeurs ont été recrutées et ont effectué 10 minutes d'enregistrement par imagerie magnétique fonctionnelle (IRMf) à l'état de repos. Les estimations de connectivité fonctionnelle de 17 RSNs extraites par une méthode de parcellisation fonctionnelle du cerveau ont été comparées entre les groupes. Le couplage entre les réseaux d'attention dorsale (DAN) et d'attention ventrale (VAN) était significativement plus élevé chez les participants qui présentent une surdité. Ces deux systèmes sont impliqués dans les tâches attentionnelles descendantes (« top-down ») et ascendantes (« bottom-up »), respectivement. Les résultats démontrent une réorganisation du cerveau au sein des réseaux associatifs et proposent une preuve potentielle des substrats neuronaux qui sous-tendraient les performances attentionnelles supérieures des personnes avec une surdité.

**Mots-clés** : IRMf ; état de repos ; surdité ; plasticité cérébrale ; connectome ; réseaux fonctionnels distribués.

# Abstract

Neural activity shared between different brain regions allows estimation of functional activation patterns at the scale of distributed networks, even in the absence of a paradigm. Consistently reported in the healthy population, resting-state functional networks (RSNs) can be studied to understand the contribution of atypical sensory development on global inter-network communication. To date, few studies have explored brain organization at rest in the context of deafness. Yet, numerous evidence supports the importance of early sensory input in the consolidation of the brain's functional architecture. The study presented in this thesis was developed and conceptualized to report on the relationship between sensory deprivation and spontaneous brain activity between RSNs. To this end, 17 individuals with severe to profound congenital hearing loss and 18 non-signer hearing individuals were recruited and performed 10 minutes of functional magnetic imaging (fMRI) recording at rest. Functional connectivity estimates of 17 RSNs extracted by a functional brain parcellation method were compared between groups. The coupling between dorsal attention (DAN) and ventral attention (VAN) networks was significantly higher in deaf participants. These two systems are involved in top-down and bottom-up attentional tasks, respectively. The results demonstrate brain plasticity within associative networks and offer potential evidence of neural substrates that may underlie superior attentional performances observed in individuals with deafness.

**Keywords:** Resting-state fMRI; Deafness; Brain plasticity; Connectome; Large-scale networks.

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### Article 1

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# Liste des sigles et abréviations

AUD : Auditory Network

BOLD : Signal dépendant du niveau d’oxygène dans le sang (de l’anglais « blood oxygen level-dependent »)

CF/FC : Connectivité fonctionnelle / Functional Connectivity

DAN : Dorsal Attentional network

DMN : Default Mode Network

HA : Hearing aid

IC/CI : Implant cochléaire / Cochlear Implant

IRM/MRI : Imagerie par résonance magnétique / Magnetic Resonance Imaging

IRMf/fMRI : Imagerie par résonance magnétique fonctionnelle / Functional Magnetic Resonance Imaging

LSQ : Langue des signes québécoises

ROI : Région d'intérêt (de l’anglais « Region of Interest »)

rs-fMRI : Imagerie par résonance magnétique fonctionnelle au repos (de l’anglais « Resting-State Functional MRI »)

RSN : Réseaux fonctionnels au repos (de l’anglais « Resting-State Network »)

SAL : Salience Network

SMN : Somatomotor Network

STG : Gyrus temporal supérieur (de l’anglais « Superior Temporal Gyrus »)

VAN : Ventral Attentional Network

VN : Visual Network

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# Chapitre 1 – Introduction

## Avant-propos

L’exposition aux expériences sensorielles façonne la trajectoire du développement cérébral. Or, les personnes privées de sens suivent un développement sensoriel atypique, qui se traduit notamment par des changements dans l’organisation structurelle et fonctionnelle du cerveau. Par exemple, en présence d’une surdité, les régions auditives s’adaptent pour traiter les entrées sensorielles provenant de différentes modalités ou substituent leur traitement sensoriel à des fonctions cognitives supérieures. Ces changements ne se limitent cependant pas aux régions de la modalité affectée, ils sont soutenus par l’ensemble du cerveau.

Les progrès réalisés dans les méthodes de neuroimagerie au cours des dernières décennies témoignent de la capacité d’adaptation du cerveau. Entre autres, l’excellente résolution spatiale de l’imagerie par résonance magnétique fonctionnelle (IRMf) permet d’explorer les corrélats neuronaux qui sous-tendent les comportements adaptatifs typiquement rapportés chez les personnes privées de sens. À ce jour, peu d’études se sont penchées sur les réseaux fonctionnels au repos (RSNs) de personnes atteintes par une surdité congénitale, i.e., depuis la naissance. Les RSNs sont des mesures robustes susceptibles d’agir comme marqueurs prédictifs de l’efficacité de la réhabilitation auditive par implant cochléaire (IC). Une meilleure compréhension des RSNs revêt un potentiel clinique important pour celleux qui désirent recourir aux dispositifs d'aide auditive. L’objectif de ce mémoire est de mieux comprendre l’impact d’une surdité congénitale sur les propriétés fonctionnelles du cerveau au repos.

Dans la section qui suit, un tour d’horizon de la surdité et de sa portée sur la neuroplasticité sera abordé sous l’angle de la neuroimagerie. Le second chapitre présentera les résultats d’une étude en imagerie par résonance magnétique fonctionnelle au repos (rs-fMRI). Les différences dans le couplage des RSNs seront examinées entre des adultes qui présentent une surdité congénitale sévère à profonde et des contrôles entendants similaires en âge, sexe et habiletés de raisonnement non verbal. Enfin, le troisième chapitre intégrera les résultats empiriques dans une discussion générale en posant un regard critique sur les limites et perspectives de recherche.

## Regard sur la surdité

Les données démographiques parlent d'elles-mêmes quant à l'importance d'étudier la privation sensorielle, plus précisément de la surdité. En effet, on estime que 5% de la population mondiale souffre de déficience auditive incapacitante (OMS; Organisation mondiale de la Santé, 2018). Au Québec, le portrait de la surdité est plus aggravant, avec un nombre qui s'élève à 17% (Statistique Canada, 2018). L'augmentation du taux de perte auditive avec l'âge (Feder et al., 2015) expliquerait la prévalence plus élevée de la province en raison du phénomène de vieillissement rapide observé dans la population québécoise (Azeredo & Payeur, 2015). L'âge d'apparition ainsi que la sévérité de la perte auditive varient toutefois selon sa cause (OMS, 2018). L'hétérogénéité des caractéristiques liée à la perte auditive trouve également écho dans la terminologie utilisée. Par exemple, une perte auditive légère à moyenne désigne une personne malentendante, tandis que le terme « sourd » s'applique lorsque le degré de perte est de niveau sévère à profond (Carbin & Smith, 2013). Les conséquences sociales et les difficultés langagières consécutives à une surdité sont intrinsèquement reliées à la sévérité de la privation sensorielle de l'individu. Il convient alors d'explorer la littérature sur les mécanismes cérébraux affectés par la surdité afin de comprendre le rôle et les implications des études en neuroimagerie pour les personnes atteintes.

## La neuroplasticité

La neuroplasticité (plasticité cérébrale ou plasticité neuronale) renvoie à la malléabilité du cerveau face aux expériences, une capacité d'adaptation présente tout au long de la vie (Oberman & Pascual-Leone, 2013). Les changements structurels et fonctionnels inhérents au processus de neuroplasticité permettent un certain retour à la normale pour les personnes ayant subi un accident ou une intervention chirurgicale. Prenons le cas des personnes épileptiques qui subissent une hémisphérectomie pour retirer un hémisphère entier et qui, quelques mois plus tard, sous l'effet de la neurogenèse, voient sur leur scan d'imagerie par résonance magnétique (IRM) un remplacement de l'hémisphère retiré. Bien que l'exemple précédent illustre les capacités d'adaptation du cerveau en termes de réorganisation des fonctions, les conséquences ne se présentent pas toujours comme étant adaptatives (Heimler et al., 2014) selon le stade de développement neurologique atteint et l'intégrité des mécanismes de régulation homéostatique (Dennis et al., 2013), par exemple.

Dit autrement, la capacité à réintégrer le traitement de la fonction privée peut être maladaptive si elle se présente inhibée pendant la réhabilitation (Singh et al., 2018). À l'inverse, la neuroplasticité peut être adaptative lorsqu'il y a facilitation du traitement des modalités sensorielles intactes ou des régions de traitement de plus haut niveau (Merabet & Pascual-Leone, 2010). L'étendue des mécanismes affectés est donc caractéristique du modèle de neuroplasticité à l'étude (Ismail et al., 2017). De fait, les changements structurels et fonctionnels qui résultent d'une privation sensorielle font l'objet d'une vaste littérature, en particulier la cécité qui le modèle de privation sensorielle le plus étudiée.

### Réorganisation du cortex à la suite d’une privation sensorielle

Certaines périodes de développement postnatales du cerveau sont caractérisées par une plus grande sensibilité aux expériences (Bruer, 2001; Kral, 2013). Durant ces périodes sensibles, l’exposition à des stimuli environnementaux est nécessaire pour consolider les circuits synaptiques et assurer un développement régulier (Chaudhury et al., 2016). L’étude d’enfants sourds implantés (e.g., Kral & Sharma, 2012; Sharma et al., 2002) a permis d’identifier la période sensible où le système auditif central est le plus réceptif au changement. Pour les personnes atteintes de surdité prélinguale qui désirent opter pour une réhabilitation auditive, l’implantation de neuroprothèse avant l'âge de 9 mois est recommandée pour un développement optimal du langage (Dettman et al., 2021), quoique d’autres auteurices soutiennent des âges plus tardifs (e.g., dans les quatre premières années; Kral & Sharma, 2012; Niparko et al., 2010). Dans tous les cas, l’absence ou la sous-stimulation d’entrées sensorielles lors de la maturation du cortex auditif impacte grandement le développement cérébral (Bavelier & Neville, 2002; Merabet & Pascual-Leone, 2010).

En fait, il serait erroné de restreindre les changements fonctionnels aux périodes de développement de bas âge. Ces modifications peuvent être induites sur de brèves périodes de privation sensorielle (Castaldi et al., 2020) ; ils se produisent dans le cerveau mature (Ismail et al., 2017; Porto et al., 2015; Voss et al., 2017) et chez les nouveau-nés qui ont eu peu d’expériences sensorielles (DeMaster et al., 2019). Pour ces derniers, même une privation sensorielle de courte durée peut laisser des traces visibles des années plus tard. Une étude (Collignon et al., 2015) s’est intéressée à la réorganisation corticale d’adultes ayant subi une chirurgie au cours de leur première année de vie pour traiter une cataracte congénitale. Une absence de stimulation visuelle entre 9 et 238 jours préchirurgie a suffi pour accroitre l’activité de régions visuelles (dans V3) lors d’une présentation de stimuli auditifs lorsque comparé au groupe contrôle. Toujours est-il que les effets à long terme d'une cécité temporaire coïncident avec l'âge de la privation. Comme le rapportent les auteurices (Collignon et al., 2015), cette nuance renvoie à l'âge précoce d'apparition de la cataracte congénitale, à la différence d'une cécité tardive qui ne génère pas le même degré de changement sur la fonction cérébrale (e.g., Voss et al., 2008) et sur les performances comportementales (e.g., Dormal et al., 2016; Oshima et al., 2014; Wan et al., 2010). En revanche, une privation sensorielle précoce entraîne des changements plastiques plus marqués, ce qui en fait un bon modèle pour étudier comment la privation sensorielle modifie le couplage d'activité neuronale du cerveau.

### La neuroplasticité intermodale

Une théorie dominante dans la littérature suggère que les aires sensorielles inutilisées peuvent être recrutées pour le traitement fonctionnel d'autres systèmes sensoriels intacts, un processus désigné par neuroplasticité intermodale (e.g., Bavelier & Neville, 2002; Bell et al., 2019; Frasnelli et al., 2011; Merabet & Pascual-Leone, 2010; Singh et al., 2018; Voss, 2019; Voss & Zatorre, 2012). Chez les personnes qui ont une surdité, cette neuroplasticité intermodale s'exprime par l'activation de régions auditives pour les entrées visuelles et tactiles (Auer et al., 2007; Bavelier et al., 2001; Bottari et al., 2014; Fine et al., 2005; Finney et al., 2001; Karns et al., 2012; Sadato et al., 2005). À proprement parler, cette théorie se manifeste au moyen de la préservation et du changement fonctionnel.

La préservation fonctionnelle propose qu'une région corticale se substitue à une autre modalité pour maintenir sa fonction (Cardin et al., 2020; Meredith et al., 2011), de sorte que le gyrus temporal supérieur (STG) postérieur, qui est associé au traitement spatial de stimuli auditifs, s'active pendant les tâches de mouvement visuel (Shiell et al., 2015), par exemple. À l'inverse, la neuroplasticité intermodale peut s'exprimer par un changement de fonction en plus de la modalité sensorielle (Cardin et al., 2020), telle qu'une réallocation du cortex temporal pour le traitement des visages (Benetti et al., 2017) et de la mémoire de travail visuel (Buchsbaum et al., 2005; Cardin et al., 2018; Ding et al., 2015). Les changements fonctionnels provoqués par la privation d'entrées auditives peuvent donc se restreindre à la substitution de modalité sensorielle ou se manifester jusqu'aux fonctions cognitives de plus haut niveau.

En conséquence, de nombreuses études se sont penchées sur l'effet compensatoire de la privation sensorielle, c'est-à-dire sur la possibilité pour les personnes atteintes de développer des « supra-performances » par l'utilisation accrue des régions auditives par d'autres modalités. Pourtant, la compilation des preuves ne converge pas vers une prémisse convaincante de capacités améliorées pour la perception tactile (Bolognini et al., 2012; González-Garrido et al., 2017; Hauthal et al., 2014; Moallem et al., 2010; Papagno et al., 2016; Sharp et al., 2020). Il semble tout de même y avoir un avantage dans la cécité lorsque les ressources attentionnelles sont concentrées sur une modalité sensorielle en comparaison aux tâches qui nécessitent une interaction entre différentes modalités (pour une revue, voir Occelli et al., 2013). En fait, l'appui favorable aux supra-performances de personnes ayant une surdité trouve son fondement en vision, en particulier lorsque la modulation attentionnelle est présente (pour des revues, voir Bavelier et al., 2006; Mitchell & Maslin, 2007; Pavani & Bottari, 2021). Le temps de réaction plus rapide pour les informations visuelles spatiales présentées en périphérie comparativement aux contrôles (Bottari et al., 2011; Chen et al., 2006; Codina et al., 2011; Codina et al., 2017; Nava et al., 2008; Prasad et al., 2017) pourrait possiblement être un avantage marqué des réponses d'orientation aux stimuli environnementaux (Pavani & Bottari, 2012).

Pour ce qui est des fonctions olfactives, les résultats mitigés sur la détection, la discrimination et l'identification d'odorants ne montrent pas de différence de taille d'effet entre les personnes voyantes et aveugles (pour une revue, voir Sorokowska et al., 2019). De plus, la littérature est très limitée concernant la privation auditive. Une étude menée dans notre laboratoire (voir Annexes pour le preprint) cherchait à comprendre l'impact de la surdité congénitale sur les capacités chimiosensorielles par le biais de tests psychophysiques. Deux mesures de la théorie de détection du signal ont été évaluées pour minimiser les problèmes liés à la prise de décision des tâches sensorielles : l'indice de sensibilité (i.e., précision avec laquelle le stimulus peut être détecté en comparant les succès et les fausses alarmes) et le biais de réponse (i.e., critère subjectif dans la réponse du participant). Nos résultats suggèrent une meilleure acuité olfactive et une plus grande sensibilité trigéminale dues à la privation sensorielle, mais aucune différence dans les schémas de réponses avec les contrôles. Ceci contraste avec les capacités diminuées précédemment rapportées chez les individus atteints de surdité (Diekmann et al., 1994; Guducu et al., 2016). Nous attribuons cette divergence à divers facteurs méthodologiques importants, tels que l'hétérogénéité des échantillons et le manque de contrôle des fonctions cognitives dans les études précédentes.

En résumé, les connaissances actuelles ne permettent pas d'affranchir un lien direct et robuste entre la neuroplasticité intermodale et les capacités sensorielles améliorées en contexte de surdité. Cependant, la neuroimagerie permet d'identifier des biomarqueurs objectifs de la neuroplasticité. Comme discuté dans le chapitre 3 de ce mémoire, comprendre les patrons d'activité cérébrale induits par l'absence de stimulation auditive est d'un intérêt clinique considérable pour améliorer les stratégies de réadaptation de personnes candidates à l'IC.

### Les bases de l'organisation cérébrale

Deux écoles de pensées concurrentes quant au rôle des fonctions cérébrales se sont imposées aux 19e et 20e siècles. Le localisationnisme, tel que proposé par les travaux de Karl Broca, défend l'emplacement des fonctions cérébrales dans des régions spécifiques et délimitées.

En aval à cette théorie, l’étude de lésions corticales chez des rats menée par Jean Pierre Flourens puis Karl Lashley fait plutôt émerger l’idée que la fonction serait distribuée à l’échelle du cerveau entier et non restreinte à une aire précise. Il est maintenant reconnu que ces deux principes, i.e. ségrégation fonctionnelle et intégration fonctionnelle, complémentent tous deux l’organisation du cerveau (Friston, 2002). Cette architecture fonctionnelle peut être répartie en réseaux locaux ou à large échelle (Varela et al., 2001). D’ordre local, la population de neurones qui composent une cytoarchitecture commune présente une activité synchrone qui s’échelonne sur de courte distance (e.g., par le biais de connexions monosynaptiques). À large échelle, les régions distales d’un réseau donné communiquent à travers un circuit de faisceaux neuronaux polysynaptiques. De fait, la ségrégation fonctionnelle propose une division du cortex cérébral en différents modules spécialisés et localisés, contrairement à son homologue d’intégration fonctionnelle qui renvoie plutôt aux interactions dynamiques entre ces modules (Eickhoff & Müller, 2015; Stephan & Friston, 2009).

La science des réseaux facilite notre compréhension de l’environnement complexe qui nous entoure, et le cerveau ne fait pas exception. Appliquées à diverses disciplines, dont le transport, la génétique et la bibliométrie, les règles mathématiques qui régissent la modélisation de réseaux trouvent également un appui dans la représentation du cerveau humain. Suivant une analogie avec le génome, le connectome est présenté comme une cartographie des réseaux de connexions du système neuronal (Sporns et al., 2005). Ainsi, le cerveau peut être décrit comme un ensemble complexe de réseaux qui suit une organisation de nœuds (de l’anglais « nodes » ; e.g., les régions cérébrales) et d’arêtes (de l’anglais « edges »), soit les connexions entre les différents nœuds. Des auteurs (Kral et al., 2016) comparent la perte sensorielle à une « maladie du connectome » en raison de la codépendance des entrées sensorielles dans le développement du connectome. Cette « maladie » affecterait le couplage entre les différents systèmes sensoriels ainsi que les voies descendantes qui accèdent au lobe temporal (Kral, 2013). L'utilisation de cette modélisation en neuroimagerie est d'un grand intérêt pour comparer les réseaux fonctionnels du cerveau.

## La connectivité fonctionnelle

Connu par son accroche « neurons that fire together, wire together » (Hebb, 1949), le postulat de Hebb indique que les évènements survenant au même moment auraient une forte probabilité d'être liés ensemble. À l'échelle macroscopique, ce principe peut s'appliquer sur la connectivité fonctionnelle du cerveau, terminologie qui désigne la corrélation temporelle entre des évènements neurophysiologiques spatialement éloignés (Friston et al., 1993; Friston, 1994). Traditionnellement mesurée avec une tâche, la covariance d'activité cérébrale entre régions distinctes se présente également en l'absence de paradigme expérimental (pour l'étude d'origine, voir Biswal et al., 1995). Les fluctuations de basses fréquences du signal BOLD qui surviennent spontanément au repos sont une propriété intrinsèque de notre cerveau (Fox & Raichle, 2007) et permettent d'inférer sur la connectivité fonctionnelle (Biswal et al., 1995).

La popularité des études en rs-fMRI est exhibée par la multiplication de publications scientifiques des dernières décennies. Plusieurs propriétés des RSNs participent à cette effervescence, notamment leur cohérence et reproductibilité élevées entre les participants et les séances et leur fiabilité test-retest modérée à élevée (Damoiseaux et al., 2006; Li et al., 2012; Wang et al., 2013; Zuo & Xing, 2014). Les régions cérébrales qui occupent un même RSN présentent un couplage fonctionnel relativement plus élevé qu'avec les régions de RSNs distincts (Biswal et al., 1995). La robustesse de cette découverte a été répliquée maintes fois depuis (e.g., Damoiseaux et al., 2006; Fox et al., 2005; Fox & Raichle, 2007). Selon la méthode d'analyse adoptée (e.g., Bellec et al., 2010; Power et al., 2011; Yeo et al., 2011), on compte aujourd'hui entre 5 et 15 RSNs (Eickhoff et al., 2018) qui présentent une grande correspondance avec l'activation cérébrale induite par des tâches (Smith et al., 2009).

De surcroit, les régions cérébrales qui composent les RSNs partagent des fonctions communes (van den Heuvel, 2010), ce qui se traduit par un chevauchement avec des réseaux fonctionnels connus. À titre d'exemple, en raison de leur fonction homologue dans le traitement de l'audition, le regroupement de régions corticales au sein du STG, soit le gyrus de Heschl, ainsi que les régions auditives primaires et associatives, forment le réseau auditif (AUD). Comme les RSNs sont systématiquement observés dans la population saine, ils sont pertinents pour identifier les différences dans l'architecture des réseaux distribués des populations cliniques. Le rs-fMRI a notamment été utilisé pour comprendre les altérations fonctionnelles induites par les maladies pédiatriques et neurologiques (Lee et al., 2013). Dans cette perspective, son application pourrait être utile pour évaluer l'organisation intrinsèque du cerveau privé d'une modalité sensorielle.

## La présente étude

Il est maintenant sans équivoque que les connexions fonctionnelles du cerveau sont altérées par la privation sensorielle. Le STG est souvent utilisé comme région d'intérêt (ROI) pour examiner l'activité cérébrale intrinsèque en raison de son importance pour le traitement auditif et langagier (Ding et al., 2016; Holmer et al., 2022; Li et al., 2019; Li et al., 2013; Xia et al., 2017). Néanmoins, les preuves examinées ici semblent suggérer une neuroplasticité intermodale qui s'exprime par des changements qui s'étayent au-delà du cortex auditif. Par exemple, le STG exhibe un couplage altéré avec les régions visuelles, qui est renforcé par des changements dans la fluctuation locale du signal BOLD (Li et al., 2019; Xia et al., 2017). Cela dit, nous en savons très peu sur la manière dont l'intégration fonctionnelle est réorganisée à plus large échelle.

Comme démontré dans ce chapitre, étudier le cerveau par le modèle du connectome devient pertinent pour comprendre comment la privation sensorielle modifie la communication entre des régions corticales spatialement distribuées. Quelques études récentes se sont penchées sur l'apport d'une surdité sur la connectivité fonctionnelle interréseaux chez les enfants (Wang et al., 2021), les adolescents (Li et al., 2015) et les adultes (Bonna et al., 2020; Ducas et al., 2021; Kumar et al., 2021). Les tendances montrent principalement une altération de la synchronie entre les réseaux visuel (VN), auditif (AUD), langagier, sensorimoteur (SMN), salience (SAL) et du mode par défaut (DMN). L'étude empirique de ce mémoire (chapitre 2) fait du pouce à cette littérature pour expliquer la contribution de l'expérience sensorielle des premiers stades de développement sur l'architecture fonctionnelle du cerveau. Plus précisément, il sera question de valider le rs-fMRI comme mesure de connectivité fonctionnelle chez des personnes atteintes de surdité congénitale afin d'élucider comment le cerveau réalloue ses fonctions communicationnelles et d'intégration en absence de stimulation auditive.

# Chapitre 2 – Article

## Contribution

Ce second chapitre présente une étude d'IRMf au repos qui s'inscrit dans un plus large projet de recherche mené au laboratoire de Franco Lepore comprenant plusieurs acquisitions de données d'IRMf de participants sourds et contrôles. La conceptualisation de ce projet a initialement été élaborée par Franco Lepore. Comme première autrice du manuscrit, Catherine Landry a complété la recension des écrits, prétraité les données, réalisé les analyses et écrit l'entièreté de l'article. Marie Simon a développé le protocole expérimental conjointement avec Franco Lepore qui a supervisé le projet de maitrise et fourni les fonds de recherche. La collecte de données a été réalisé par Marie Simon.

# Large-scale brain network alterations during rest in congenital deafness

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## Abstract

Sensory deprivation is associated with widespread brain reorganization. This study aims to investigate large-scale brain network alterations induced by early hearing loss using resting-state functional MRI (rs-fMRI). Individuals with severe-to-profound congenitally deafness (*n* = 17) and age– and sex–matched hearing non-signers (*n* = 18) were recruited and underwent 10-minute recordings at rest. Mean connectivity estimates of 17 resting-state networks (RSNs) were compared between groups. We found that the coupling patterns of spontaneous brain activity between dorsal attention (DAN) and ventral attention (VAN) networks were significantly increased in deaf participants. These neural systems are involved in top-down and stimulus-driven attentional tasks, respectively. Despite being typically associated with altered functional processing in deafness, no evidence was found for other RSNs, including the somatomotor, auditory, visual, frontal and default mode networks. Together, these results demonstrate the degree of complexity and variability at which cross-modal plasticity alters the functional integration of the brain. These findings also provide neural substrates that may underlie superior attentional performance in deaf individuals.

*Keywords*: Resting-state fMRI; Brain plasticity; Connectome; Large-scale networks; Deafness

# Introduction

Hearing loss during the early sensitive period induces distinct changes in the structural and functional organization of the brain. Various findings suggest that deafness-induced neuroplasticity can either preserve or alter the function of the sensory-deprived cortices (for a review, see Cardin et al., 2020). That is, auditory-related areas adapt to process sensory inputs from different modalities (Auer et al., 2007; Bavelier et al., 2001; Bottari et al., 2014; Fine et al., 2005; Finney et al., 2001; Karns et al., 2012; Sadato et al., 2005) or substitute their sensory processing for higher cognitive functions, such as face processing (Benetti et al., 2017), visual working memory (Buchsbaum et al., 2005; Cardin et al., 2018; Ding et al., 2015), and visual attention (Bavelier et al., 2000). Moreover, cross-modal plasticity manifests through functional processing alterations that extend beyond the temporal lobe (e.g., Bavelier & Neville, 2002; Bell et al., 2019; Merabet & Pascual-Leone, 2010). For instance, the superior temporal gyrus (STG) exhibits increased activity during visual motion tasks (Shiell et al., 2015) and impaired coupling with visual regions (Kumar et al., 2021), which is further supported by changes in local blood oxygen level-dependent (BOLD) signal oscillations (Li et al., 2019; Xia et al., 2017). Numerous morphological studies also demonstrate changes in nonauditory areas (for reviews, see Grégoire et al., 2022; Simon et al., 2020), thereby reinforcing whole-brain reorganization upon sensory deprivation.

Resting-state functional MRI (rs-fMRI) measures low-frequency fluctuations in the BOLD signal to assess estimates of intrinsic neural activity that occurs spontaneously at rest, commonly referred to as functional connectivity (FC) (Biswal et al., 1995; Buckner et al., 2013). Its applicability has been popularized in recent decades, whereby the functional architecture of the brain reveals an organization into a complex set of resting-state networks (RSNs) with underlying neuroanatomical connections (De Luca et al., 2006; Greicius et al., 2009). RSNs are also known to mirror task-oriented cerebral activation patterns (Smith et al., 2009; Thomas Yeo et al., 2011). Hence, the representation of the human brain can be studied through the connectome lens, i.e., the mapping of the neural system into interconnected networks (Sporns et al., 2005). Given the codependence of sensory inputs with the development of the connectome, some authors (Kral et al., 2016) compare sensory deprivation to a "connectome disorder" that affects the coupling between different sensory systems, along with top-down pathways passing through the temporal lobe (Kral, 2013). As they are consistently reported in healthy populations (Fox & Raichle, 2007), RSNs are relevant in understanding how atypical sensory development alters communication among large-scale functional brain networks.

Researchers have recently shown interest in rs-fMRI to examine intrinsic brain activity associated with deafness. Using independent component analysis (ICA) to identify RSNs, previous studies found increased inter-network connectivity namely between somatomotor network (SMN), auditory network (AUD), visual network (VN), and frontal networks (FN) in the congenitally deaf (Kumar et al., 2021; Wang et al., 2021), although alterations of intrinsic brain activity in the default mode network (DMN) only emerged in male adults (Kumar et al., 2021). Similar results were shown in other studies using different brain parcellation methods (Bonna et al., 2020; Dell Ducas et al., 2021). Decreased coupling patterns relative to control seemed prominent in frontal areas (Li et al., 2015), between salience networks (SAL) and language networks (Dell Ducas et al., 2021). Specific nodes are also linked to altered FC, namely in the left middle temporal gyrus and right hemispheric regions such as superior gyrus, insula, and posterior cingulate gyrus (Li et al., 2015). The posterior cingulate cortex and the medial prefrontal cortex nodes within the DMN also present altered coherent brain activity with visual and motor networks (Dell Ducas et al., 2021).

Overall, these studies suggest distributed functional changes due to early deafness, with patterns of hypo- and hyper-connectivity in both sensorimotor and associative networks. However, methodological and sampling variability between studies makes it difficult to capture consistent patterns at the network level. With no means to compare methodological differences between data-driven and model-based, we rather add to the previous studies investigating FC measures using a parcellation-based connectome analysis. Our study used the Yeo atlas which can extract either 7 or 17 RSNs yielding stable parcellation (Sadato et al., 2005). Given that the high number of participants in the atlas construction is the most significant correlate of inter-atlas similarity (Doucet et al., 2019), Yeo's atlas offers a compelling advantage for its use of a large sample size (*n* = 1000).

To this end, we used rs-fMRI to examine the coupling patterns of spontaneous brain activity between large-scale networks in adults with congenital severe-to-profound hearing loss compared to hearing non-signers. Given the cross-modal plasticity with visual and somatosensory processing, we expect inter-network changes in FC measures in sensorimotor networks (SMN, AUD, VN). Furthermore, evidence favorably supports supra-performance in deaf individuals in the visual modality, particularly when attentional modulation is involved (Bavelier et al., 2006; Mitchell & Maslin, 2007; Pavani & Bottari, 2021). Therefore, we hypothesized that higher-level association RSNs will also exhibit altered functional connections, including SAL, DMN, attention networks.

## Methods

### Participants

Seventeen severe-to-profound prelingually deaf adults were recruited through certified audiologists at the Raymond Dewar Institute in Montreal based on a bilateral hearing loss greater than 77 dB (right ear: *M* = 94, *SD* = 10.74, range = 70-115; left ear: *M* = 95.47, *SD* = 8.94, range = 77-110). Additionally, 18 hearing non signers were recruited from the University of Montreal and the Montreal Metropolitan area. The two groups did not differ in age and had similar gender distribution (Table 1). Given the lateralization of cerebral functions, the handedness of all participants was assessed using the Edinburgh Handedness Inventory Index (Oldfield, 1971). All participants were screened for normal or corrected vision and no history of neurological or psychiatric disorders. Control participants had no history of hearing disorder or sign language knowledge. Information on history of hearing loss, means of communication and use of hearing aid was collected through a self-reported questionnaire. Out of the 17 deaf individuals, 9 used spoken French as their primary language and were wearing a hearing aid (HA) at the time of testing and 8 communicated preferably with sign language (LSQ; Langue des Signes Québécoise), 4 of them being native signers. The etiology of the deafness was unknown for 11 participants, 4 had hereditary deafness, and 2 were caused by meningitis.

Differences in functional networks have been reported in relation to intelligence (Song et al., 2008; 2009; Van Den Heuvel, 2009). Measures of nonverbal intelligence are essential for assessing cognitive function in deaf individuals (Zekveld et al., 2007), as they avoid confounding language with intellectual abilities and penalizing deaf individuals who have atypical language development. Nonverbal fluid reasoning (Strauss et al., 2006) was measured by the Matrix Reasoning subtest of the Weschler Abbreviated Scale of Intelligence, Second Edition (WASI-II; Wechsler & Hsiao-pin, 2011) as a measure for cognitive function with good high interrater reliability (0.99; McCrimmon & Smith, 2013). Both the control and the deaf groups scored in the medium to the superior level compared to normative data. Descriptive statistics of participants are presented in Table 1.

Table 1. Descriptive statistics of participant demographics

| | Participants | | Statistics |
|---|---|---|---|
| | Hearing non-signers (n=18) | Congenitally deaf (n=17) | |
| Age | | | U = 138.5, P-value = 0.636 |
| Mean (SD) | 29.89 (5.27) y | 30,35 (4.57) y | |
| Range | 22-37 y | 21-37 y | |
| Sex, n (%) | | | X2 = 0.151, P-value = 0.697 |
| Female | 13 (72.22) | 12 (70.59) | |
| Male | 4 (22.22) | 5 (29.41) | |
| Handedness | | | X2 = 0.245, P-value = 0.621 |
| Right | 15 (83.33) | 12 (70.59) | |
| Left | 3 (16.67) | 5 (29.41) | |
| Non-verbal IQ score | | | t(33) = 2.117, P-value = 0.406 |
| Mean (SD) | 30.28 (2.39) | 28.35 (2.83) | |
| Years of education | | | U = 216.5, P-value = 0.035* |
| Mean (SD) | 16.94 (1.66) y | 15.29 (2.42) y | |

*Note*: SD, Standard Deviation; y: years. $*p < 0.05$

This study was approved by the ethics committee and scientific boards of the Centre de Recherche Interdisciplinaire en Réadaptation du Montréal métropolitain (CRIR) and the Quebec Bio-Imaging Network (QBIN). All participants enrolled voluntarily and gave written informed consent. Participation was rewarded with monetary compensation.

## MRI data acquisition

MRI data were acquired using a 3-T Trio Tim system (Siemens Magnetom, Erlangen, Germany) equipped with a 32-channel head coil as previously described (Campbell, 2022; Simon et al., 2020). High resolution T1-weighted (T1w) structural images were collected using a MPRAGE sequence (voxel size = 1.0 × 1.0 × 1.0 mm; TR/TE = 2300/2.98 ms; TI = 900 ms; FA = 9°; FOV = 256 x 256 mm; 192 sagittal slices). Whole brain T2*-weighted images were obtained using a gradient echo-planar imaging (EPI) sequence with the following parameters: voxel size = 3.0 x 3.0 x 3.2 mm; TR/TE = 2200/30 ms; FA = 90°; FOV = 64 x 64 mm; 35 axial slices in interleaved ascending order; interslice gap = 4 mm. We acquired 274 volumes for each functional run. Signal inhomogeneity correction was accounted for with B0 mapping sequence using the slice position and resolution of the EPI acquisition (TE 1 = 4.92 ms; TE 2 = 7.38 ms; 37 slices). Head movements were restrained with foam pads. The rs-fMRI acquisition had a duration of 10 min, during which each participant was instructed to lie still with their eyes closed and to avoid falling asleep or holding on to thoughts.

## MRI pre-processing

The dataset was first standardized according to the Brain Imaging Data Structure (BIDS) specifications (Gorgolewski et al., 2016) to facilitate reproducibility and run BIDS supported software's. Full documentation on the BIDS structure can be found at https://bids.neuroimaging.io. Data was then preprocessed using fMRIPrep (v. 21.0.1; Esteban et al., 2018a; 2018b) based on Nipype (v. 1.6.1; Gorgolewski et al., 2011; 2018). Many internal operations of fMRIPrep use Nilearn (v. 0.8.1; Abraham et al., 2014), mostly within the functional processing workflow. For more details of the pipeline, see the section corresponding to workflows in fMRIPrep's documentation (https://fmriprep.org/en/latest/workflows.html).

### Anatomical Preprocessing

T1-weighted volumes were corrected for intensity non-uniformity using N4BiasFieldCorrection (Tustison et al., 2010) using ANTs 2.3.3 (Avants et al., 2008) and skull-stripped via a brain extraction procedure using the OASIS template. Brain tissue segmentation of cerebrospinal fluid (CSF), white-matter (WM) and gray-matter (GM) was performed on the brain-extracted T1w using FAST (FSL v. 6.0.5.1; Zhang et al., 2001). Spatial normalization to

MNI standard space was performed through nonlinear registration with ANTs (v. 2.3.3), using brain-extracted versions of both T1w reference and the T1w template (ICBM 152 Nonlinear Asymmetrical template version 2009c; Fonov et al., 2009).

### Functional Preprocessing

A fieldmap was estimated from the phase-drift map measure with two consecutive GRE (gradient-recalled echo) acquisitions and were phase-unwrapped with prelude (FSL). For the preprocessing of functional images, a reference volume and its skull-stripped version were generated with a custom fMRIPrep methodology. Head-motion parameters (transformation matrices, and six corresponding rotation and translation parameters) were estimated with mcflirt in FSL (Jenkinson et al., 2002). The fieldmap run was aligned with rigid registration to the target EPI reference run and the field coefficients mapped on to the reference EPI using the transform. BOLD runs were slice-time corrected to 1.07s (0.5 of slice acquisition range 0s-2.15s) using 3dTshift from AFNI (Cox & Hyde, 1997). The BOLD reference was then co-registered to the participant's corresponding T1w reference using bbregister (FreeSurfer) and configured with six degrees of freedom.

Several confounding time-series were calculated based on the preprocessed BOLD: framewise displacement (FD), DVARS and three region-wise global signals. FD was computed using two formulations: absolute sum of relative motions (Power et al., 2014) and relative root mean square displacement between affines (Jenkinson et al., 2002). FD and DVARS are calculated for each functional run, both using their implementations in Nipype (following the definitions by Power et al., 2014). The three global signals are extracted within the CSF, the WM, and the whole-brain masks. The confound time series derived from head motion estimates and global signals were expanded with the inclusion of temporal derivatives and quadratic terms for each (Satterthwaite et al. 2013). FD > 0.5 mm or standardized DVARS > 1.5 were annotated as motion outliers. All transformations (i.e., head-motion transform matrices, susceptibility distortion correction, and co-registrations to anatomical and output spaces) were resampled using antsApplyTransforms (ANTs) with Lanczos interpolation when volumetric and using mri_vol2surf (FreeSurfer) when surface-based.

### Quality Assessment

As recommended for a fMRI workflow protocol (Esteban et al., 2020), MRI data quality control was assessed with MRIQC (v. 0.16.1; Esteban et al., 2017). MRIQC is an open-source tool that extracts image-quality metrics (IQM) and generates visual summary reports to facilitate the screening of anatomical and functional data. Outliers can be easily flagged by visual inspection. There is currently no consensus on benchmark rules for excluding poor quality data. Hence, no participants were excluded solely based on the MRIQC quality assessment reports (see Data availability below for data sharing agreement).

### Functional Connectomics Analysis

The Python package Nilearn (http://nilearn.github.io) was used for confounds regression, FC estimation, and data visualization. The denoising strategy included 24 motion estimates (6 translations/rotations, 6 temporal derivatives, 6 quadratic terms, 6 square of derivatives) and 8 physiological parameters (extracted from the means of WM and CSF signals). Non-steady volumes were also discarded. Next, a Gaussian kernel of 6 mm full width at half maximum (FWHM) was applied, along with a 0.01–0.08 Hz band-pass filter to remove low frequency drift from scanner instabilities and high-frequency physiologic noise. The functional images were then parceled into 17-cluster RSNs using a deterministic atlas template (Yeo et al., 2011). Of particular interest to the functional processing affected in deafness, we chose the fine-resolution map rather than the 7-networks parcellation map to further divide the association networks (frontoparietal control and default) and the sensorimotor networks (visual and somatomotor). Connectivity profiles can be sufficiently differentiated to be fractioned into smaller subnetworks. As such, we avoid averaging time courses of regions involved in distinct information streams.

The mean timeseries were extracted to compute a 17x17 correlation matrix (289 correlation coefficients) for each participant. Individual matrices were then averaged for between-group comparisons. The absolute values of skewness for both matrices respected the normality criterion of < 2 (see Additional Material) as proposed by West et al. (1996). Kurtosis is only valid for n >= 20. Therefore, the tail distribution of the data was not considered a reliable measure of normality given our sample size. Pearson correlations were then z-scored to fit the data to a Gaussian distribution, an underlying statistical assumption for parametric tests. An independent two-sample t-test was conducted to compare functional connectomes between deaf and hearing individuals. The *p*-values were determined using permutations as it does not make strong assumptions about the shape of the underlying distribution. Significant inference was set at $p < 0.05$ with Bonferroni correction.

Within-group analyses were also performed to ascertain data comparability given the heterogeneity of the deaf sample. Namely, functional connectomes of deaf individuals wearing a HA at the time of testing ($n = 9$) were compared with those who had no HA experience ($n = 8$). A similar comparison was performed for LSQ users ($n = 8$) and those who preferentially communicate with the oral modality ($n = 9$). No significant difference was observed between those comparisons (Bonferroni corrected at $p < .05$, threshold = 3.452).

## Results

We compared functional connections by measuring pairwise correlations between the correspondent time series of 17 RSNs. Among these comparisons (Bonferroni corrected at $p < .05$, threshold = 3.452), a significant increase of medium effect size ($r = 0.51$) in the coupling of ventral attention (VAN) and dorsal attention (DAN) networks was found in deaf individuals compared to controls ($t(33) = -3.45$, $p = .00$). The VAN comprised the following cortical regions: parietal operculum, medial parietal, medial frontal, precentral ventral frontal, insula, temporal, precentral frontal, posterior temporal. Whereas the DAN includes the posterior temporal occipital, the superior parietal, and the inferior parietal occipital. Between-group differences are presented in Figure 1.

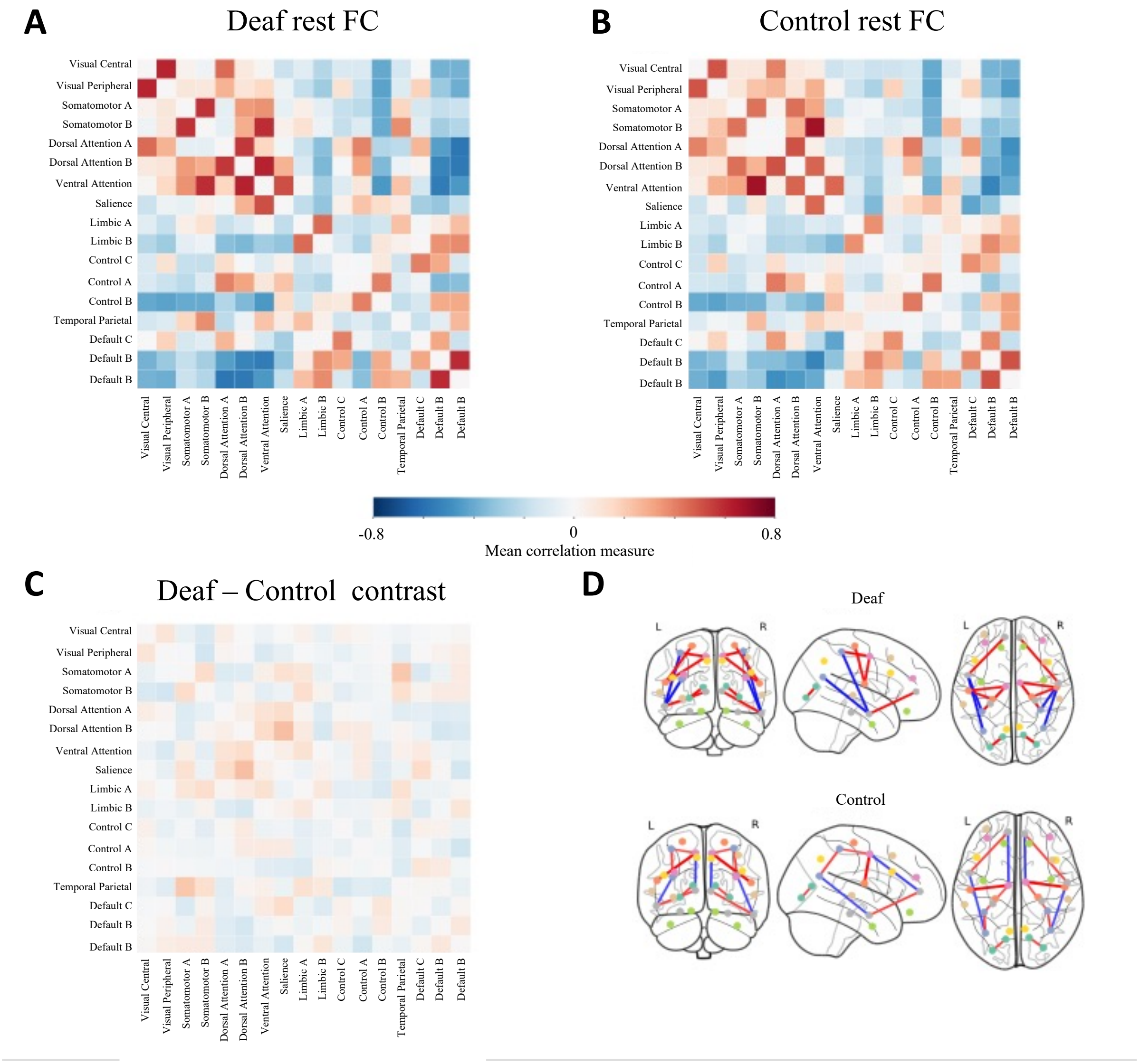

**Figure 1.** Group analysis of rs-fMRI connectivity between congenitally deaf individuals and non-signers hearing controls. Mean correlation matrix for (A) deaf participants (*n* =17) and (B) control participants (*n* = 18). (C) Subtraction between deaf and control connectivity matrices. The significance level of brain activation is indicated by the color bar, with red for increased and blue for decreased activity. (D) Cortical surface plot showing 95% of edge strength connectivity.

# Discussion

In this study, we investigated functional brain organization in individuals with congenital deafness during rs-fMRI. Time series were extracted using a parcellation strategy of 17 RSNs (Yeo et al., 2011) and then computed in the connectivity domain for between-group comparisons. Increased internetwork connectivity was detected in deaf individuals between VAN and DAN. This result corroborates that early sensory deprivation induces functional changes at the network level. Contrary to expectations, we did not find widespread connectivity alterations between the SMN, AUD, VN, and FN. Instead, we found that lack of auditory stimulation in early years selectively encompasses inter-network plasticity in neural systems involved in attentional tasks.

## Role of attentional modulation in deafness

Results show altered connectivity restricted to the VAN-DAN coupling, with increased FC in deaf individuals. VAN is associated with bottom-up attention processes (Corbetta et al., 2008), which are best described by reorienting behaviors toward salient features (e.g., color, motion, luminance). Alternatively, DAN is implicated with top-down, goal-oriented processes (Corbetta et al., 2008; Fox et al., 2005). Despite visual enhancement being identified in tasks that do not require selective attentional resources (Alencar et al., 2019), evidence generally implicates modulatory allocation of selective visual attention (e.g., Bavelier et al., 2006; Mitchell & Maslin, 2007; Pavani & Bottari, 2012). Some authors have proposed that the enhancement of selective visual attention in deafness, probably adaptative, could originate from functional and structural specificities of the parietal attention network (Dye et al., 2007). The demonstration of such cognitive demands stems primarily from face and motion processing. For example, when evaluating whether the upper and lower halves of a face belonged to the same person (composite face), deaf individuals outperformed controls (Mitchell & Letourneau, 2013). One possible explanation might relate to increased attention to information in this area. Moreover, apparent motion presented peripherally increased the functional connections between motion selective areas with the posterior parietal cortex and the superior temporal sulcus in deaf signers (Bavelier et al., 2001). Specific patterns of network alterations may thus contribute to adaptive behaviors relating to sensory deprivation.

However, the substantial evidence suggesting selective attention allocation does not clearly differentiate between exogenous and endogenous orientation (Pavani, & Bottari, 2012). As reported by the authors, future studies should define the attentional stream being studied to allow for a better understanding of the tasks susceptible to elicit deafness-induced neuroplasticity. This could have implications for our results, as it is difficult to relate which aspects of visual attention enhanced behaviorally could potentially reflect patterns of resting-state. As mentioned earlier, large scale functional networks reflect task-oriented cerebral activation patterns (Smith et al., 2009; Thomas Yeo et al., 2011) and share as much as half its variance to stimulus-evoked activity (Cole et al., 2014). It is important to bear in mind that the definition of modules in connectivity-based parcellation, though defined as functional regions, rely on shared statistical associations between homogeneous regions and are not synonymous with function.

Moreover, we interpret the increase FC between DAN and VAN as a possible explanation for why deaf individuals perform better than controls in some attentional tasks. It is worth mentioning that a higher FC could indicate greater redundancy in the information shared between distributed brain regions. This opposing view has been advanced particularly in motor learning tasks. For example, one study investigated whether antidepressant medication would alter brain connectivity when paired with motor learning of implicit sequence (Molloy et al., 2021). After 7 days of medication intake, results showed a decrease in connectivity between the thalamus and motor regions. The authors explain this decrease as an improvement in network-level processing efficiency during sequential motor learning. Similarly, another study has also demonstrated an association between decrease functional integration of motor-related networks and motor learning tasks (Coynel et al., 2010). In relation to our study, this could suggest that deaf individuals require more resources in terms of DAN and VAN interactions to outperform controls. Further research is needed to confirm the link between behavior and connectivity to advance such claims.

### Lack of cross-modal plasticity in sensorimotor networks

Perhaps the most counterintuitive finding is the absence of significant results for sensorimotor networks, given previous evidence (Bonna et al., 2020; Dell Ducas et al., 2021; Kumar et al., 2021; Wang et al., 2021). Several factors could explain this observation as there are many approaches available to divide the brain into subnetworks. Compared to previous studies, we applied a surface-based functional parcellation that divides the brain into functional units to describe deafness-related cortical network changes. This method is useful for mapping macroscopic connectomes (de Reus & Van den Heuvel, 2013) but as a downside, statistical inferences about the functional properties of networks are greatly influenced by the parcellation approach (Gordon & Laumann, 2016). A study evaluating spatial variability between the most reported RSN in the literature (Doucet et al., 2019) revealed that RSN defined by atlases with the same label shared as little as 39% of similarity. Variability between subjects also demonstrates that inconsistency may be due to the overlapping of regions between different networks (Yeo et al., 2014).

Previous studies demonstrated altered FC in deafness with nodes located in the temporal and cingulate gyrus (Dell Ducas et al., 2021; Li et al., 2015). These regions participate in multiple RSNs, specifically the associative networks. Therefore, although the appellations are dissimilar across studies, it is best to evaluate whether there is convergence of the same regions through various studies. The inherent intersubjective variability of higher-level networks may explain why our finding is less replicated in previous studies. Atlas construction should therefore stem from larger samples as it increases inter-atlas similarity and provides a more reliable and stable parcellation solution (Doucet et al., 2019). A stamping of 100 individuals has been proposed for improved inter-atlas similarity (Doucet et al., 2019). We counterbalanced this limitation by using an atlas constructed with a clustering algorithm applied to rs-fMRI recordings of 1000 individuals. This makes it a good candidate for reliability across studies.

## Limitations

The generalizability of these results is subject to certain limitations. First, the sample size is relatively small in both groups, although comparable to previous studies. For instance, sample sizes of deaf individuals included in a recent review on structural plasticity range from 6 to 92 with an average of 24 individuals (Simon et al., 2020). However, the small number of participants contributes to sampling variability that may hinder the detection of group differences. Future studies would benefit from more reliable FC estimates and increased statistical power for better reproducibility (Button 2013; Chen & Yan, 2018) with a larger sample size. Another alternative is to consider Bayesian inference, a mathematical approach capable of discriminating between the likelihood of the null hypothesis (no effect) and lack of statistical power (no evidence) (Keysers et al., 2020). To date, only one known study has applied both Bayesian and frequentist inferences in deafness (Campbell, 2022). This application could prove to be a cornerstone for future analyses in research areas, such as sensory deprivation, where data are unlikely to reach the optimal sample size (Cardin et al., 2020) identified with power analysis, for example.

In addition, audiologic information and means of communication were not examined in the scope of our study. HA influence the degree of residual hearing by amplifying ambient noise. Recent studies have shown reverse temporal recruitment during a visual task (Glick & Sharma, 2020) and altered functional connections to the visual cortex (Shiell et al., 2015), with only about two weeks of HA use sufficient to generate neural changes in auditory areas (Karawani et al., 2022). A decrease in FC between the auditory cortex and fusiform gyrus has also been reported in age-related hearing loss after six months of HA use (Rosemann et al., 2021). Although sparse, evidence suggests an effect of residual hearing on cortical reorganization. HA duration was not explored in our study. However, within-group analyses revealed no significant differences in the functional connectomes of HA users versus non-users. In future studies, deaf individuals using HA should be treated as a separate group given the association of auditory experience with the degree of neuroplasticity. Unfortunately, aided threshold information was unknown for our participants, half of whom were wearing a device at the time of the experiment. Assessment of HA functional gain is relevant as HA improves residual hearing and, consequently, the adaptive component of neuroplasticity.

Furthermore, our study was unable to differentiate functional changes inherent to language proficiency from early sensory deprivation. Visuospatial language (sign language) influences the organization of neural systems, as demonstrated in motion tasks (e.g., Bavelier et al., 2001; Simon et al., 2020) and hemispheric laterality (e.g., MacSweeney et al., 2004). These functional changes could potentially translate into RSNs architecture. The deaf individuals included in our sample communicated either in the oral modality or in sign language. No differences were found between the functional connectomes of oral communicators and signers, hence the rationale for using only one experimental group to obtain a larger sample size. This methodological choice is itself problematic in that it infers the comparability of deafness characteristics. For our study, deaf participants with HA who use an oral mode of communication were grouped with deaf signers who have no auditory input from HA. Such grouping compromises the potential effect or interaction between different confounding variables. When possible, future studies should investigate sign language users separately from those who communicate with spoken language to disentangle language plasticity (Que et al., 2018). A group of hearing signers (e.g., born to deaf parents and/or raised in a signing community) could further highlight the effects of sign language acquisition regardless of auditory experience.

## Conclusion

Determining the impacts of sensory deprivation on FC measures is of great interest to the understanding of cross-modal neuroplasticity operating in the early sensitive period. Our study revealed an increased coupling between VAN and DAN in participants with congenital deafness. This finding endorses the association between sensory deprivation and altered communication among large-scale brain networks, as measured with resting-state FC. Most notably, it highlights the involvement of higher-level cognitive function networks at rest.

**Data availability:** With respect to patient confidentiality, the metadata and MRIQC quality assessment can be made available upon request to the corresponding authors.

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## Additional Material

Table 2. Skewness values for the matrix of deaf participants

| **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9** | **10** | **11** | **12** | **13** | **14** | **15** | **16** | **17** | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | -0,98 | 0,28 | -0,37 | -0,53 | -0,95 | -0,04 | -0,83 | 0,17 | -0,19 | -0,34 | 0,28 | 0,39 | 1,43 | 0,37 | -0,10 | 0,43 | **1** |
| | | 0,44 | -0,20 | -0,72 | -0,05 | 0,36 | 0,30 | 0,37 | -1,16 | -0,59 | -0,30 | 0,93 | 0,77 | -0,39 | -0,34 | 0,03 | **2** |
| | | | -0,91 | -0,72 | 0,30 | -0,13 | 0,63 | -0,40 | 0,03 | -0,16 | 0,69 | 0,69 | -0,36 | -0,55 | 0,52 | 0,12 | **3** |
| | | | | -0,61 | -0,66 | -1,52 | 0,39 | -0,11 | 1,07 | 0,84 | 0,01 | 0,55 | -0,84 | -0,58 | 1,00 | 0,72 | **4** |
| | | | | | -0,24 | -0,41 | -0,04 | 0,75 | -0,09 | -0,17 | 0,10 | 0,42 | 0,09 | -0,34 | -0,24 | 0,34 | **5** |
| | | | | | | -0,25 | 0,30 | 0,14 | 0,36 | 0,48 | -0,22 | 0,57 | -0,71 | -1,04 | 0,34 | 0,05 | **6** |
| | | | | | | | -0,28 | -0,51 | -0,12 | 0,04 | -0,32 | 0,52 | -0,46 | -0,40 | 1,18 | -0,59 | **7** |
| | | | | | | | | -0,23 | 0,25 | -0,02 | -0,20 | -0,29 | -0,20 | 0,87 | 0,00 | -0,23 | **8** |
| | | | | | | | | | 0,00 | 0,12 | 1,24 | 0,41 | 0,17 | -0,43 | -0,38 | 0,22 | **9** |
| | | | | | | | | | | 0,27 | 0,48 | 1,24 | -0,08 | -0,72 | -0,88 | 0,13 | **10** |
| | | | | | | | | | | | -0,51 | 0,00 | 0,83 | -1,05 | -0,46 | 0,58 | **11** |
| | | | | | | | | | | | | -0,56 | 0,00 | 0,09 | 0,32 | 0,77 | **12** |
| | | | | | | | | | | | | | 0,05 | 0,40 | -0,59 | -0,42 | **13** |
| | | | | | | | | | | | | | | -0,25 | 0,14 | -0,11 | **14** |
| | | | | | | | | | | | | | | | -0,13 | 0,06 | **15** |
| | | | | | | | | | | | | | | | | 0,09 | **16** |
| | | | | | | | | | | | | | | | | | **17** |

*Note:* The 17 networks from the Yeo atlas are identified as follows: (1) Central visual; (2) Peripheral visual; (3) Dorsal somatomotor; (4) Ventral somatomotor; (5) Posterior dorsal attention; (6) Somatomotor association; (7) Posterior ventral attention; (8) Anterior ventral attention; (9) Medial temporal–limbic; (10) Orbitofrontal–limbic; (11) Medial superior parietal; (12) Medial frontoparietal; (13) Lateral frontoparietal; (14) Lateral temporal–default mode network (DMN); (15) Ventral–DMN; (16) Dorsal–DMN; and (17) Lateral–DMN.

Table 3. Skewness values for the matrix of hearing participants

| **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9** | **10** | **11** | **12** | **13** | **14** | **15** | **16** | **17** | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | -0,70 | 0,18 | -0,26 | -0,83 | 0,34 | -0,33 | -0,07 | -0,36 | 0,66 | 0,57 | 0,05 | 0,89 | 0,51 | 0,31 | 0,01 | 0,51 | **1** |
| | | -0,53 | -0,19 | 0,02 | 0,17 | -0,13 | -0,06 | -0,44 | -0,20 | -0,13 | -0,34 | 0,39 | 0,51 | 0,08 | -0,25 | 0,72 | **2** |
| | | | -0,03 | 0,07 | -0,24 | -0,68 | 0,01 | -0,07 | -0,06 | -0,42 | 0,35 | 0,37 | 0,21 | 0,34 | -0,28 | 0,37 | **3** |
| | | | | -0,17 | 0,06 | -0,25 | 0,06 | -0,35 | 1,04 | -0,29 | 0,35 | 0,47 | -0,23 | 0,97 | 0,01 | 0,31 | **4** |
| | | | | | -1,20 | -1,41 | 0,25 | -0,34 | 0,36 | 0,13 | -1,08 | 1,13 | -0,11 | 0,34 | 0,84 | 0,97 | **5** |
| | | | | | | -1,43 | 0,38 | -0,45 | -0,20 | 0,30 | 0,20 | -0,15 | 0,18 | -0,36 | 0,59 | 0,90 | **6** |
| | | | | | | | 0,34 | -0,40 | 0,10 | 0,41 | -0,43 | -0,97 | -0,04 | -0,03 | 1,64 | 1,20 | **7** |
| | | | | | | | | 0,58 | 0,35 | -0,06 | -0,49 | -0,08 | 0,09 | 0,42 | -0,10 | 0,34 | **8** |
| | | | | | | | | | -0,29 | 0,08 | -0,38 | -0,76 | -0,15 | -0,33 | 0,78 | -0,31 | **9** |
| | | | | | | | | | | -0,14 | 0,00 | 0,50 | -0,57 | -0,21 | -0,32 | 0,13 | **10** |
| | | | | | | | | | | | -0,31 | -0,34 | 0,09 | -0,16 | -0,23 | -0,55 | **11** |
| | | | | | | | | | | | | -0,09 | 0,36 | 0,28 | 0,26 | 0,97 | **12** |
| | | | | | | | | | | | | | -0,66 | 0,20 | -0,60 | -0,09 | **13** |
| | | | | | | | | | | | | | | -0,62 | 0,01 | -0,01 | **14** |
| | | | | | | | | | | | | | | | 0,39 | 0,60 | **15** |
| | | | | | | | | | | | | | | | | -0,13 | **16** |
| | | | | | | | | | | | | | | | | | **17** |

*Note:* The 17 networks from the Yeo atlas are identified as follows: (1) Central visual; (2) Peripheral visual; (3) Dorsal somatomotor; (4) Ventral somatomotor; (5) Posterior dorsal attention; (6) Somatomotor association; (7) Posterior ventral attention; (8) Anterior ventral attention; (9) Medial temporal–limbic; (10) Orbitofrontal–limbic; (11) Medial superior parietal; (12) Medial frontoparietal; (13) Lateral frontoparietal; (14) Lateral temporal–default mode network (DMN); (15) Ventral–DMN; (16) Dorsal–DMN; and (17) Lateral–DMN.

# Chapitre 3 – Discussion Générale

## Contributions de l'étude : ce que révèlent les données

Les différentes conditions de développement cérébral atypique alimentent un intérêt particulier dans la communauté scientifique. L'absence ou l'exposition sous-optimale aux expériences sensorielles altère à la fois le fonctionnement cérébral des aires sensorielles et des aires cognitives de haut niveau, et ce, de l'enfance à l'âge adulte. Malgré la malléabilité du cerveau, la neuroplasticité est directement liée au degré de sévérité de la perte auditive et de l'audition résiduelle. La surdité congénitale de degré sévère à profond bilatéralement est un modèle robuste pour étudier l'étendue des changements dans l'organisation fonctionnelle qui sont associés à la privation sensorielle. Compte tenu de ce qui précède, l'étude présentée dans ce mémoire a été conceptualisée et réalisée pour approfondir notre compréhension des substrats neuronaux altérés à l'échelle du cerveau lorsque l'expérience auditive est minimale. Les fluctuations spontanées du signal BOLD qui surviennent en l'absence de paradigme expérimental ont servi d'estimation de la connectivité fonctionnelle entre les différents RSNs.

Les résultats de notre étude ont d'abord montré une relation fonctionnelle altérée entre VAN et DAN chez les personnes ayant une surdité en comparaison aux contrôles entendants. Ces réseaux fonctionnels sont associés aux processus d'attention ascendants et descendants (Corbetta et al., 2008), respectivement. Ce résultat est cohérent au principe de plasticité intermodale selon lequel la privation sensorielle précoce induit des changements fonctionnels qui s'étayent au-delà du cortex auditif (Bavelier & Neville, 2002; Bell et al., 2019; Merabet & Pascual-Leone, 2010). À cet égard, il apparaît particulièrement intéressant de considérer l'implication des résultats sachant qu'une perte auditive en bas âge modifie certains aspects de l'attention visuelle (e.g., Dye et al., 2007). Diverses preuves soutiennent une attention visuelle sélective accrue en fonction de la surdité (par exemple, Bavelier et al., 2006 ; Mitchell & Maslin, 2007 ; Pavani & Bottari, 2012). En lien avec les réseaux fonctionnels à grande échelle, jusqu'à la moitié de la variance du signal BOLD en l’absence de paradigme expérimental (Cole et al., 2014) reflète les schémas d'activation cérébrale induite par une tâche (Smith et al., 2009 ; Yeo et al., 2011). On peut alors supposer une possible contribution des schémas d’activations des réseaux fonctionnels aux comportements adaptatifs liés à la privation sensorielle.

Contre toute attente, le patron d’hyperconnectivité entre les réseaux sensorimoteurs VN et SMN identifié dans plusieurs études (Bonna et al., 2020; Dell Ducas et al., 2021; Kumar et al., 2021; Wang et al., 2021) n’était pas assez robuste pour survivre aux comparaisons multiples. Outre les facteurs discutés dans la prochaine section, ceci pourrait être attribuables aux différences méthodologiques avec les études antérieures. Nous avons notamment utilisé une parcellisation fonctionnelle (Thomas Yeo et al., 2011) par opposition à l’identification de RSNs par l’ICA ou à l’application d’un atlas anatomique (e.g., Kumar et al., 2021; Li et al., 2015; Wang et al., 2021). La parcellisation du cerveau en 17 RSNs (plutôt que 7) a été appliqué en raison de la résolution fine des réseaux d'association qui sont pertinents pour la surdité. Bien qu’utiles pour cartographier les connectomes macroscopiques (de Reus & Van den Heuvel, 2013), les méthodes de parcellisation influencent les inférences statistiques des propriétés fonctionnelles des réseaux (Gordon & Laumann, 2016). Une étude (Doucet et al., 2019) évaluant la variabilité spatiale parmi les RSNs les plus rapportés dans la littérature a révélé que les RSNs définis par différents atlas ayant la même labellisation partageaient aussi peu que 39% de similarité. Par exemple, les nœuds situés dans les gyrus temporal et cingulaire qui présentent un couplage modifié chez les personnes avec une surdité (Dell Ducas et al., 2021 ; Li et al., 2015) chevauchent de multiples RSNs (Yeo et al., 2014). Par conséquent, il serait préférable d'évaluer la similarité des régions atteintes pour contrer les appellations dissemblables de RSNs entre les études.

L'administration d'une évaluation cognitive adaptée aux personnes avec une surdité constitue un avantage marqué de notre étude. De plus en plus de preuves attribuent une corrélation entre les habiletés intellectuelles et les mesures de connectivité. Ce lien est particulièrement important avec les réseaux fonctionnels à large échelle (Song et al., 2008; Van Den Heuvel et al., 2009), d'autant plus que certains réseaux agissent comme des prédicteurs de l'intelligence (Song et al., 2009). Sachant que les mesures d'intelligence non verbale départagent les capacités langagières et intellectuelles, il est possible d'évaluer les fonctions cognitives sans pénaliser les personnes ayant un développement atypique du langage (Zekveld et al., 2007). C'est pourquoi nous avons mesuré le raisonnement fluide non verbal (Strauss et al., 2006) par le subtest de la matrice de l'échelle abrégée d'intelligence de Weschler, deuxième édition (WASI-II ; Wechsler & Hsiao-pin, 2011). Les participants ont obtenu des scores se situant dans la tranche moyenne à supérieure relativement aux données normatives, sans différence de groupe significative. Le rôle de cette variable confondante se voit ainsi minimisé dans les résultats. À notre connaissance, une seule étude en rs-fMRI a mesuré l'intelligence non verbale des participants avec surdité (Kumar et al., 2021). Toutefois, leur échantillon est composé uniquement d'hommes, ce qui constitue un biais important pour la généralisation des résultats.

Enfin, il convient de souligner que le présent manuscrit s'inscrit dans le cadre d'analyses conjonctives de réseaux fonctionnels et structurels. Le même échantillon a également été étudié pour le mouvement biologique (Simon et al., 2020) et pour quantifier la structure des faisceaux de matière blanche (Campbell et al., en préparation). Ensemble, cette pluralité d'études dresse un tableau unifié des différents aspects de la connectivité chez un bassin d'individus présentant des caractéristiques audiologiques et langagières identiques. Mis à part une étude qui a simultanément évalué l’intégration fonctionnelle et structurelle dans la modélisation de réseaux chez les mêmes participants (Dell Ducas et al., 2021), l’utilisation de comparaisons multimodales en neuroimagerie reste largement inexplorée. Pourtant, une connectivité structurelle élevée corrobore avec les estimations de connectivité fonctionnelle des mêmes régions cérébrales (Damoiseaux & Greicius, 2009). Une suite conséquente au projet serait de mettre en relation les résultats de connectivité estimés indépendamment (Campbell et al., en préparation ; Simon et al., 2020) ou d’utiliser une modélisation conjointe des circuits structurels sous-jacents à la fonction, pour laquelle l’applicabilité aux RSNs semble prometteuse (pour un exemple d'application, voir Chu et al., 2018).

## Limites et perspectives dans la recherche en surdité

Sans être exhaustive, cette section détaille certains facteurs qui limitent la portée des résultats de la recherche en surdité. Plus précisément, l’hétérogénéité des échantillons, la puissance statistique et la variabilité individuelle seront abordées.

### Hétérogénéité des échantillons

Une limite récurrente dans la littérature est la difficulté à différencier les effets qui relèvent de la privation sensorielle de ceux attribuables au mode de communication. Appariés à des personnes entendantes qui ne recourent pas à la langue des signes, les signeurs natifs avec surdité constituent l’échantillon par excellence pour évaluer les effets de la privation auditive lorsque les facteurs confondants sont réduits (Bavelier et al., 2006). À l’inverse, les différences qui surviennent entre les signeurs et les non signeurs, indépendamment de leur expérience auditive, sont évocatrices des effets relevant de l’acquisition d’une langue des signes (e.g., Stroh et al., 2022). Cette distinction se constate dans diverses tâches, y compris l’avantage marqué des personnes qui ont une surdité pour le traitement périphérique, lequel ne se retrouve pas chez les entendants signeurs (e.g., Bavelier et al., 2001; Fine et al., 2005). Faute de l'hétérogénéité de l'échantillon d'individus sourds (9 oraux et 8 signeurs, dont 4 natifs) et de l'absence d'un groupe contrôle entendant fluide en LSQ, notre étude ne permet pas de dégager les changements fonctionnels inhérents au langage de la privation auditive. Bien qu'il s'agisse d'une limitation, une attention exclusivement dirigée sur les particularités de la neuroplasticité des signeurs natifs sourds soulève des préoccupations quant à la généralisation des résultats, puisqu'ils représentent un sous-groupe minoritaire de la communauté sourde (Bavelier et al., 2006).

Outre le degré de sévérité, les prothèses auditives influencent le degré d'audition résiduelle et par l'entremise, la composante adaptative de la neuroplasticité. Les appareils auditifs amplifient les bruits environnants et les transmettent à l'oreille par le biais d'écouteurs. Le nombre d'années d'utilisation affecterait l'organisation des régions auditives, de sorte qu'une durée soutenue accentue l'ampleur des changements fonctionnels, en particulier les connexions avec le cortex visuel primaire (Shiell et al., 2015). En dépit de l'utilisation variable de l'appareil, son implication dans la neuroplasticité n'est pas négligeable puisqu'elle conduirait à de meilleurs résultats après l'implantation cochléaire (Santarelli et al., 2008). Une étude (Glick & Sharma, 2020) a évalué l'effet du port d'appareils auditifs chez des personnes présentant une perte auditive liée à l'âge. Le recrutement du cortex temporal identifié durant une tâche visuelle (sans appareil) s'est inversé après l'usage régulier du dispositif sur une période de six mois, ce qui coïncide également avec la récupération de la perception de la parole. Une utilisation aussi courte que deux semaines serait même suffisante pour générer des changements neuronaux dans les régions auditives (Karawani et al., 2022).

Au regard de ces preuves, une limitation importante de notre étude repose sur le choix méthodologique d'inclure dans un même échantillon des individus sourds signeurs qui n'ont aucune entrée auditive et des individus sourds porteurs d'aide auditive et qui utilisent un mode de communication oral. Un tel regroupement est problématique dans la mesure où il compromet la découverte d’effets ou d’interactions inhérents aux caractéristiques de la surdité (e.g., mode de communication et utilisation d’appareil auditif). Les futures études bénéficieraient également à évaluer le gain fonctionnel des participants appareillés pour connaitre l’apport adaptatif de la neuroplasticité. Cette information est manquante pour la moitié de notre échantillon qui était appareillé au moment de l’expérimentation.

### Puissance statistique

Le manque de puissance statistique est un enjeu majeur pour la reproductibilité en neuroimagerie (Button 2013; Chen & Yan, 2018). Un petit échantillon augmente forcément la probabilité de détecter de faux négatifs et laisse les vrais effets passer sous silence (Button et al., 2013; Ioannidis, 2005). Il va sans dire que cela a une incidence considérable sur la variabilité de l’échantillonnage et par conséquent, sur la représentativité des résultats à l’ensemble de la population. En ce sens, des études ont cherché à savoir dans quelle mesure la taille de l’échantillon affecte les estimations de connectivité fonctionnelle. En analysant la fiabilité, la sensibilité et la valeur prédictive positive de banques de données publiquement disponibles, il en ressort que des groupes d’au moins $n = 40$ sont nécessaire pour repérer des tailles d’effet intéressantes (Chen & Yan, 2018; Gauter et al., 2018). Cet enjeu a gagné en importance au regard d’une récente publication qui a provoqué des remous dans la communauté scientifique. Dans cette étude (Marek et al., 2022), les auteurices indiquent qu’une taille d’échantillon atteignant les milliers de participants est exigée pour obtenir des résultats robustes et réduire les biais (e.g., l’inflation des tailles d’effet). Déterminer au mieux l’échantillon adéquat pour la reproductibilité des associations statistiques à l’échelle du cerveau fait encore débat et sera tout particulièrement à surveiller afin d’améliorer les bonnes pratiques de recherche en neuroimagerie.

De fait, il est à noter que l'étude présentée dans ce mémoire (Chapitre 2) est sujette à cette limitation importante, d'où l'importance d'interpréter les résultats avec prudence. La variabilité d'échantillonnage peut entraver la détection des différences inter-groupes et imputer sur la généralisation des résultats. En dépit de l'échantillon relativement petit de notre étude, la taille est comparable à celle d'études antérieures qui ont identifié des effets de groupe après corrections multiples (e.g., les études portant sur la plasticité structurelle ont en moyenne 24 individus avec surdité dans leur échantillon ; Simon et al., 2020). Sous prétexte que la complexité du processus de recrutement des populations cliniques justifie généralement le faible nombre de participants, il serait envisageable de réaliser une méta-analyse sur la connectivité fonctionnelle liée à la surdité pour dégager les tendances statistiques et évaluer si les différentes études fournissent des estimations fiables. Une plus grande taille d'échantillon profiterait également à d'autres applications analytiques, d'autant que les suggestions visant à privilégier les effets intrasujet gagnent progressivement du terrain en IRMf (e.g., Chen & Yan, 2017; Dubois & Adolphs, 2016).

### Variabilité individuelle

Bien que la variabilité individuelle soit constatée en neuroimagerie dans l'architecture structurelle du cerveau et les estimations de connectivité fonctionnelle (Gu & Kanai, 2018; Pernet et al., 2015), ceci n'a pas encore été évalué en rs-fMRI en contexte de privation sensorielle. Une étude comparant l'activité cérébrale spontanée dans 7 RSNs a identifié les réseaux associatifs comme démontrant la plus grande variabilité fonctionnelle inter-sujet, soit les réseaux attentionnels et frontopariétal (Yeo et al., 2014). Ces réseaux longent le lobe préfrontal latéral et la jonction temporo-pariétale et sont typiquement recrutés pour les fonctions cognitives supérieures. La variabilité inhérente des réseaux de plus haut niveau pourrait expliquer pourquoi le couplage altéré entre VAN et DAN rapporté dans notre étude a été peu répliqué dans les études antérieures.

Il convient également de mentionner que les méthodes de parcellisation du cerveau au niveau du groupe “moyennent” les caractéristiques de l’organisation cérébrale qui sont propres à chaque individu. Il est donc difficile, voire impossible, d’extraire les profils fonctionnels des caractéristiques individuelles liées à la surdité (e.g., la modalité langagière et l’utilisation de prothèse auditive) qui varient considérablement dans les échantillons. Des études sur des données d’IRMf ont montré que les analyses inter-groupes basées sur une parcellisation du cerveau ne détectaient pas certaines propriétés fonctionnelles présentes à l'échelle individuelle (e.g., Gordon et al., 2017; Laumann et al., 2015). Des enregistrements de plus longue durée permettraient d’extraire des estimations de connectivité fiables pour évaluer la variabilité individuelle (Gordon et al., 2017). En partant de ce principe, on peut supposer que les RSNs qui présentent une plus grande variabilité fonctionnelle individuelle révèleront également un plus grand degré de neuroplasticité durant la réhabilitation auditive.

## Implications cliniques potentielles

Divers degrés de réhabilitation auditive sont envisageables au moyen de dispositifs portatifs. L’implant cochléaire (IC) est présentement le moyen le plus efficace pour restaurer partiellement l’audition et la perception de la parole des personnes qui ont une surdité profonde. Cette prothèse neurale stimule le nerf auditif en convertissant les stimuli sonores captés par des électrodes en signaux électriques interprétables par le cerveau (Merzenich et al., 1973). La littérature soutient l’influence de l’âge d’implantation sur les performances auditives (Niparko et al., 2010), et par conséquent, qu’une implantation précoce dans l’enfance entraine de meilleures performances (Kral et al., 2013). Tout cela considéré, la période sensible du développement auditif et langagier est un facteur important dans le contexte d'interventions neuromodulatrices telles que l'IC (Ismail et al., 2017).

En revanche, des problèmes persistent dans la réhabilitation par IC. En effet, les performances auditives avec le port d'IC sont variables et l'on sait très peu sur les facteurs qui contribuent à son efficacité. Les facteurs proposés comme prédicteur de la perception auditive post-implantation représentent moins de 25% de la variance des résultats (Moberly et al., 2016). Cette faible proportion reflète un manque de cibles d'intervention viables pour les candidats d'implant. Une avenue de recherche intéressante pour pallier ce manque repose sur le postulat que la privation auditive génère une réorganisation cérébrale. À l'appui de cet argument, les preuves de changements fonctionnels et structurels induits par la surdité indiquent des répercussions sur la réhabilitation auditive avec l'IC (Lee et al., 2007; Han et al., 2019; Sun et al., 2021), en particulier lorsqu'ils se produisent dans le système auditif central (Tang et al., 2017). Les études récentes chez les animaux et les humains atteints de surdité prélinguale nuancent la contribution négative de la plasticité intermodale sur la perception de la parole post-implantation (Glennon et al., 2020). La question de savoir si la réorganisation sensorielle suivant une perte d'audition représente une bonne ou une mauvaise adaptation demeure toutefois inconcluante.

Une meilleure compréhension de la plasticité intermodale aurait donc des implications importantes sur les stratégies de réhabilitation auditive (Heimler et al., 2014), et par extension, pour l'intégration sociale et la qualité de vie des personnes concernées. À cet égard, notre étude a utilisé des données d'IRMf au repos comme marqueur objectif de l'activité cérébrale afin d'examiner la valeur ajoutée de ce marqueur en contexte de surdité. Une application potentiellement intéressante serait d'utiliser le signal BOLD qui survient spontanément au repos avant implant afin de prédire l'efficacité des prothèses neurales, en particulier pour les réponses comportementales auditives et de perception du langage. Des contrastes d'activation cérébrale en

IRMf mesurés avant l'implantation cochléaire ont notamment été utilisés pour la classification des performances linguistiques post-implant chez des enfants sourds (Tan et al., 2015). Le score de prédiction élevé du classificateur semi-supervisé démontre le possible recours aux schémas d'activation corticale comme biomarqueurs qui sous-tendent la récupération de l'audition. En revanche, la littérature en surdité sur le rs-fMRI révèle une disparité interétude qui ne permet pas d'extraire un modèle de prédiction claire pour la performance de l'IC. Quoi qu'il en soit, des études longitudinales sont nécessaires pour évaluer la pertinence de ce marqueur en contexte de réhabilitation auditive, avec une attention particulière à la variabilité individuelle attribuable à la fonction cérébrale.

# Chapitre 4 – Conclusion

Comment le cerveau se réorganise-t-il en l'absence de stimulation sensorielle ? Cette question peut être interprétée et investiguée de multiples façons. Les méthodes d'imagerie cérébrale permettent d'identifier l'architecture des réseaux fonctionnels du cerveau pour comprendre la contribution d'un développement sensoriel atypique sur la communication interréseau. À cet effet, la surdité est un bon modèle de privation sensorielle. Une personne ayant une perte auditive de degré sévère percevra très difficilement une conversation. Lorsque la perte auditive est profonde, les bruits forts tels que les alarmes à feu peuvent même être imperceptibles. Ce mémoire a donc pour objectif d'explorer les réseaux fonctionnels distribués avec l'IRMf au repos chez des adultes ayant une surdité congénitale de degré sévère à profond.

Parmi les 17 RSNs identifiés par une méthode de parcellisation fonctionnelle du cerveau, le couplage entre VAN et DAN a montré une connexion fonctionnelle accrue en comparaison aux participants contrôles. Ce résultat dénote un impact sélectif de la plasticité intermodale sur les systèmes impliqués dans les tâches attentionnelles. Il est intéressant de soulever un potentiel lien entre les substrats neuronaux activés au repos et les performances attentionnelles supérieures observées dans les études antérieures. D'autres études sont cependant nécessaires pour confirmer une corrélation comportementale et neurologique. En regard à la littérature, nous montrons également que le choix d'approche pour la définition des RSNs module les estimations de connectivité fonctionnelle au niveau des analyses de groupes. Une meilleure compréhension de l'organisation cérébrale passe par l'évaluation des paramètres méthodologiques et des caractéristiques cliniques qui expliqueraient la variabilité inter-étude.

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# Annexes

## Article supplémentaire

L'article qui suit présente un projet mené au cours de la maitrise, conjointement avec le projet de recherche principal de ce mémoire. Il s'agit d'une étude comportementale qui évalue les capacités des systèmes olfactif et trigéminal en contexte de surdité, par le biais de tests psychophysiques.

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## Contribution

Comme premières autrices, Catherine Landry et Rim Nazar ont contribué également au manuscrit. Plus précisément, Catherine Landry a participé aux analyses, à la visualisation des données, ainsi qu'à l'écriture et la révision du manuscrit. Rim Nazar a mené l'investigation auprès des participants qui vivent avec une surdité et a écrit la première ébauche du manuscrit. Marie Simon et François Genest ont tous deux contribué à la conceptualisation et aux choix méthodologiques du design expérimental. Fanny Lécuyer Giguère a récolté les données auprès des participants contrôles. Johannes Frasnelli s'est impliqué aux stades de : conceptualisation des idées, développement de la méthodologie, provision de ressources matériels, gestion de conservation des données et de l'administration du projet et révision des écrits et des analyses. Ensemble avec Franco Lepore, ils ont co-supervisé la réalisation du projet et fournis les fonds de recherche.

# Behavioral Evidence for Enhanced Olfactory and Trigeminal Perception in Congenitally Deaf Individuals

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*Keywords*: Deaf, Olfactory Perception, Trigeminal, Adaptation

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## Abstract

Sensory deprivation, particularly hearing loss, is an excellent model to study neuroplasticity in the human brain and the adaptive behaviors that support the daily lives of deprived individuals. In adaptation to their hearing loss, deaf individuals rely on their other intact senses. Visual and tactile abilities are enhanced in deafness, but few studies have evaluated the olfactory function. This study aimed to compare the impact of congenital deafness on olfactory capacities using psychophysical tasks. Methodological issues raised in previous studies, such as homogeneous onset of deafness and cognitive function assessment, were considered. Eleven individuals with bilateral severe-to-profound deafness since birth were compared to 11 hearing non-signers similar in age (age range = 20-51 years old) and sex (7 women). The deaf subjects were assessed using various standardized neuropsychological tests to ascertain typical cognition. Olfactory functions were evaluated using the Sniffin' Sticks battery test, which measures olfactory detection threshold, odor discrimination, and odor identification. Further, accuracy and response time were examined for the identification and localization of two odors to disentangle olfactory sensitivity from sensitivity in the trigeminal system. The Sniffin' Sticks test demonstrated superior performances in the deaf participants to discriminate and identify odors. In line with this, they also showed higher sensitivity when both identifying and localizing odors. These findings suggest that congenital deafness is associated with superior performance in higher-level olfactory processing and increased sensitivity in the trigeminal system.

*Keywords*: Deaf, Olfactory Perception, Trigeminal, Adaptation

## Introduction

One approach to study neuroplasticity in the human brain and related adaptive behavior is through sensory deprivation. Adaptive behaviors support the daily life of individuals deprived of a sensory modality such as hearing using the other, intact senses (Alencar et al., 2019; Bavelier & Neville, 2002; Bell et al., 2019; Pavani & Bottari, 2012). Consequently, sensory loss plays a central role in the reorganization of functional processing in the intact sensory modalities, well known as neuroplasticity. Various animal (e.g., Lomber et al., 2010), psychophysical tasks (e.g., Megreya & Bindemann, 2017; Smittenaar et al., 2016), and brain imaging studies (e.g, Simon et al., 2020) demonstrate enhanced visual performances in the congenitally deaf. Although limited, the literature regarding the tactile modality presents superior sensitivity in relation to deafness when complex and cognitive tactile processes are studied (Sharp et al., 2020; van Dijik et al., 2013). Performance enhancement related to intermodal recruitment of the auditory and other sensory areas support the hypothesis of compensatory neuroplasticity. Active regions or pathways of the brain extend at the cost of less engaged regions or pathways (Rauschecker, 1995). Therefore, like these two modalities, it can be hypothesized that hearing loss also leads to enhancement of olfactory function. Hence, this study aims to evaluate if congenital deafness induces behavioral differences in olfactory and trigeminal abilities in comparison to hearing pairs.

To date, there is a general lack of studies that quantified chemosensory abilities of deaf individuals. Previous research showed reduced performance in profound hearing-impaired adults (Diekmann et al., 1994) and congenitally deaf adolescents (Guducu et al., 2016). However, a delay in language acquisition in deaf individuals might have influenced their understanding of the tasks, especially the congenitally deaf (Diekmann et al., 1994). In turn, congenitally deaf exhibit distinct cognitive abilities, such as a better capacity to direct visual attention during tasks (Colmenero et al., 2004; Parasnis & Samar, 1985) and better spatial memorization with deaf signers compared to hearing non-signers (Cattani & Clibbens, 2005). However, control for cognitive function was not included in earlier studies on olfactory ability in deaf individuals. This is crucial as olfactory tasks such as odor identification and discrimination are intrinsically associated with proficiency in executive functioning and semantic memory across the adult life span (e.g., Hedner et al. 2010; Larsson et al., 2000).

Another shortcoming in the literature is the predominance of olfactory dysfunction. Out of the thirteen deaf participants in one study (Guducu et al., 2016), three presented normosmia (normal olfaction), seven met hyposmia clinical criterion (reduced odor detection) and two participants ranked with anosmia (loss of smell). Although participants had taken an otorhinolaryngological examination to ensure the exclusion of sinonasal pathologies and nasal septal deviation, the prevalence of olfactory impairment is higher than expected in the population (Yang & Pinto, 2016), that is, 15% cases of hyposmia and 5% anosmia (Landis et al., 2009). What remains unclear is to what extent the poor scoring reported on psychophysical tasks relate to hearing loss, higher order cognitive deficiency/proficiency, inadequate sampling or, a possible lack of understanding the task instructions by the deaf sample (Guducu et al., 2016). In short, current knowledge regarding olfactory acuity in deafness is limited by significant methodological factors, such as heterogeneous clinical scoring and deafness onset, as well as lack of cognitive function measures. The duration of deafness and auditory rehabilitation by means of a cochlear implant (CI) are also factors known to influence the extent of neuroplasticity in impaired hearing individuals (Kral et al., 2016). Consequently, these factors were considered in the present research protocols.

Pure odorants that exclusively stimulate the olfactory system are rare. When evaluating the sense of smell, odorants most likely to be found in the environment are good experimental stimuli to use. However, most odorants have mixed olfactory-trigeminal components that can be detected even by individuals with anosmia (Doty et al., 1978). The trigeminal system processes sensations such as burning, cooling, itching, or stinging evoked my volatile substances (Laska et al., 1997). Only activation of the trigeminal nerve makes it possible to localize odors (Frasnelli et al., 2007; Frasnelli et al., 2009; Kleemann et al., 2009) i.e., determining which nostril is stimulated during monorhinal stimulations. In fact, chemical (as well as thermal) stimulation of the trigeminal nerve activates different polymodal ion channels from the transient receptor potential (TRP) subfamily (Frasnelli & Manescu, 2017; Viana, 2011). For example, cooling sensation induced by cool temperatures or chemical agents such as eucalyptol (eucalyptus) activate the TRPM8 receptor (Behrendt et al., 2004; Boonen et al., 2016). Other molecules stimulate the TRPA1 receptor, ranging from benzaldehyde (almond-like odor) (Richards et al., 2010) to various other irritants (Viana, 2011). In addition to its adaptative and protective functions for localizing potentially dangerous external stimuli, the trigeminal system plays an important role in the overall chemosensory experience. It may therefore be conceivable that trigeminal sensitivity is increased in congenitally deaf individuals. However, trigeminal sensitivity in deaf individuals has not yet been investigated.

This study explored olfactory and trigeminal processing behaviorally in congenitally deaf individuals. Specifically, detection threshold, discrimination and identification of odors was assessed, combined with a task of timed odor localization and identification. Addressing previous methodological limitations and controlling for cognitive function, olfactory performance is expected to be enhanced in individuals with congenital deafness given the crossmodally adaptative neuroplasticity in sensory deprivation. In line with visual and tactile performance, congenitally deaf individuals should manifest superior olfactory performances. This difference should extend to the trigeminal system, with deaf individuals presenting better ability to localize odors.

## Materials & Methods

### Participant Characteristics

Twenty-two participants took part in this study: 11 individuals [male = 4, female = 7; age range = 20-51 years (*M* = 35.64; *SD* = 9.63)] with severe-to-profound bilateral congenital hearing loss assessed by audiologists and 11 hearing non-signers [male = 4, female = 7; age range = 20-52 years (*M* = 35.64; *SD* = 10.42)]. The cause of deafness was sensorineural for all 11 deaf individuals. Experimental and control groups were matched for sex and age. Only individuals with a normal sense of smell were included (combined threshold-discrimination-identification (TDI) score ≥ 31/48). Individuals with psychiatric or neurological disorders (Moberg et al., 1999; Moscavitch et al., 2009), otolaryngology disease associated with olfactory dysfunctions (Landis et al., 2009), and smokers (Vennemann et al., 2008) were excluded. Every participant was instructed to avoid eating an hour before the experiment and were prohibited to use scented products on the day of testing. The study was approuved by the Research Ethics Board of the Centre de Recherche Interdisciplinaire en Réadaptation du Montréal métropolitain (CRIR) and the Centre de Recherche de l'Hôpital Sacré-Coeur de Montréal. All participants enrolled voluntarily and gave written informed consent. Participation was rewarded with monetary compensation. Table 1 presents the sociodemographic characteristics of all the participants.

[Insert Table 1]

#### ***Cognitive Assessments***

Given previous studies that suggest differential cognitive abilities in the deaf, cognitive function was ascertained in these participants by administering a series of validated non-verbal neuropsychological tests. Specifically, they included (1) spatial memorization capacities and visuo-constructive skills, specifically planning capacity, organizational skills, and perceptual and motor functions with the *Rey-Osterrieth Complex Figure test* (Deborah & Jane, 1985); (2) visuospatial and visuomotor coordination skills with the Blocks subtest and visuoperceptual and logical reasoning skills with the Matrix subtest of the *Wechsler Abbreviated Scale of Intelligence II* (Wechsler, 2013); and (3) ability to orient and maintain an adequate and stable level of efficiency throughout a visual activity with *Ruff 2 & 7 test* (Ruff et al., 1992). Each percentile rank score was within average when compared to the normative samples of the respective tests. More precisely, deaf individuals had average Z-scores for the Rey-Osterrieth Complex Figure test in immediate recall (Z = -0.67), delayed recall (Z = -0.6), and recognition (Z = 0.2), the Blocks test (Z = 1.09), the Matrix test (Z = 0.87) and the Ruff 2 & 7 test, both in accuracy (Z = -0.6) and speed (Z = 0.24) within the normative average.

### Procedure

Deaf participants were recruited through program managers, audiologists, and billboard advertisements at the Institut Raymond-Dewar of Montreal. The hearing participants were recruited online or through notices posted on the University of Montreal billboards. Control participants were chosen according to their age and sex to allow matching with deaf individuals. Information related to hearing loss, medical history and demographic information was collected through emails to ensure compliance with the inclusion criteria of the study. To address potential communication difficulties and promote optimal participation of deaf signers, a Quebec sign language (LSQ) interpreter translated the task instructions and the research protocol into LSQ.

Videos of the interpreter were presented to the deaf participants before each tasks using a touchpad. The experimenter also communicated with the deaf participants through paper writing until complete understanding. Instructions were given verbally to the control participants.

### *Questionnaires*

A short questionnaire was designed to ascertain the participants' demographic information (education, age, sex). Deaf participants also filled two other questionnaires concerning their hearing impairment history (etiology, onset of deafness, duration of hearing loss, CI usage) and their means of communication (age exposure to language, oral fluency, and sign language).

### *Olfactory Function Assessment*

Olfactory capacities were evaluated with the Sniffin' Sticks test (SST; Burghardt, Wedel, Germany) (Hummel et al., 1997). This 40-to-60-minute validated task (Kobal et al., 2000; Hummel et al., 2007) uses a set of felt-tip pen-like odor dispensing devices – the Sniffin' Sticks – designed to release odors at increasing intensity/different quality and evaluates threshold detection (T), discrimination (D) and identification (I) of odors. Three scores ranging from 1 to 16 were obtained for each condition. The TDI score (Wolfensberger, 2000) ranks the performance on a clinical scale from 1 to 48: normosmia ($TDI \geq 31$), hyposmia ($15 < TDI < 31$) and anosmia ($TDI \leq 15$) (Hummel et al. 2007; updated version Oleszkieicz et al., 2019). Participants were blindfolded to avoid visual identification of odors through stimulus recognition. After each trial, participants were asked to validate the response written on paper. The following sections briefly detail the assessment procedure of each subtask (for more details, see Rumeau & Jankowski, 2016).

1- The *detection* threshold (T) was assessed with a 3 multiple forced choice following an ascending/descending staircase procedure to 16 triplets of sticks. For each trial, three sticks were presented (20 seconds each) in random order, two containing a solvent and the third containing a diluted concentration of phenylethanol alcohol (PEA, rose-like odor) according to predefined degrees. Participants were asked to identify the PEA stick within the triplets. Two consecutive correct identifications of the PEA stick reverse the staircase to a lower concentration staircase. An error reverses the scale to a higher concentration staircase. The test ends when the scale reversal criterion is encountered seven times. The detection threshold score was defined as the mean of the last four staircase turns (Hummel et al., 2007).

2- The *discrimination* task (D) uses 16 triplets of sticks randomly presented, two sticks containing the same odorant and a third one containing the target odorant (Hummel et al. 2007). Participants were asked to determine which of the three sticks smelled differently. Each triplet was separated by at least 30 s and each stick presentation was separated by a 3 s interval. The discrimination score results in the sum of correctly identified odd sticks.

3- The odor *identification* (I) was carried out using a 4 multiple-forced choice where the participant had to correctly identify 16 sticks containing different common odors (Hummel et al. 2007). Participants could freely smell as much as considered necessary before answering. Each stick presentation was separated by a 30 s interval. The identification score is defined by the sum of correctly identified odors.

### ***Automated Odorant Localization and Identification (AOLI)***

A computer-controlled device delivering fast and stable stimulus (Lundström et al., 2010) was used to measure the identification and localization of odors. A total of 36 stimulations were presented: 12 air (control), 12 benzaldehyde [almond (A); Sigma–Aldrich, St. Louis, MO, USA] and 12 eucalyptol [eucalyptus (E); Galenova, St.-Hyacinth, QC, Canada] stimuli. Benzaldehyde and eucalyptol were chosen because they are mixed olfactory-trigeminal stimuli, i.e., they stimulate both the olfactory and the trigeminal system. Both benzaldehyde and eucalyptol were diluted at 50% in propylene glycol (Sigma–Aldrich, St. Louis, MO, USA). Stimulations were delivered in a randomized order through one of the two nostrils: [left (L) or right (R)] every 30 s. On half of the trials, the participant was asked the command "Where?" (localization of the stimulated nostril, R or L; forced choice); the other half they were asked the command "What?" (identification of the delivered stimuli, A or E; forced choice) before odorant delivery via computer screen (Kéïta et al., 2013). By doing so, sensitivity in the trigeminal system (odor localization) and in the olfactory system (odor identification) were assessed. The participants were instructed to press the adequate keyboard button as fast as possible. The number of hits (correct detection when the stimulus is present), false alarms (inaccurate detection of the stimulus when absent) and response time (in seconds) was measured. To avoid habituation, stimuli were separated by a 40 s fixed interval and conditions were counterbalanced. A white noise was continuously played to cover the sounds emitted by the device to prevent cueing the localization or identification of odorants. This preventive procedure was perpetuated in the deaf group for protocol standardization purposes.

The sensitivity index *d'* and response bias *C* were then computed based on the number of hits and false alarms (Stanislaw & Todorov, 1999). In Signal Detection Theory, the sensitivity index represents the accuracy with which the stimulus can be detected by comparing hits with false alarms. The higher the values of *d'*, the better the task was performed. The response bias *C* indicates the participant's subjective criterion for responding: a positive bias reveals a tendency either towards a side (localization task) or stimulus (identification task).

## Statistical Analyses

Data was analyzed with SPSS (version 27 for macOS 10.14+, SPSS Inc., Chicago, IL). Sphericity (Mauchly's test of Sphericity, $p > 0.05$), normality (Kolmogorov-Smirnov test for normality, $p > 0.05$) and variance homogeneity (Levene's test, $p > 0.05$) postulates can be assumed for SST and AOLI scores data.

An independent sample *t*-test was performed to compare the computed TDI score between deaf and hearing individuals. A repeated-measures analysis of variance was next carried out (rm-ANOVA) to compare the effect of *condition* (between-subject factor; 2 levels: deaf, hearing) on scores with *task* (3 levels: detection, discrimination, identification) as within-subject factor. For the AOLI scores, the dependent variables sensitivity index and response bias were submitted to a rm-ANOVA with *task* (2 levels: identification, localization) as within-subjects factor and *condition* (2 levels: deaf, control) as between subjects factor.

Finally, mean scores (SST, AOLI) were subjected to the Mann-Whitney *U* test to compare deaf individuals wearing a CI at the time of testing with those who have no CI experience. All post-hoc comparisons were corrected with Bonferroni's procedure. The alpha level of significance was set at 0.05 for all analyses.

# Results

## Olfactory Function Assessment

On average, deaf participants ($M = 40.159$, $SD = 3.204$) obtained a higher global TDI score than control individuals ($M = 36.204$, $SD = 3.409$). This difference (95% CI, 0.270-2.096) was significant, $t(20) = -2.803$, $p = 0.011$ with a high effect size, $d = 1.195$.

With regards to the individual tests of the SST, the rm-ANOVA revealed no statistically significant interaction between *task* * *condition* ($F(2,40) = 0.463$, $p = 0.633$, $\eta^2 = 0.23$). A significant main effect of *condition* was observed ($F(1,20) = 7{,}859$, $p = 0.011$, $\eta^2 = 0.282$), with deaf individuals outperforming controls, in line with the result of the global TDI score. Finally, we observed a significant main effect of *task* ($F(2,40) = 9.795$, $p < 0.001$, $\eta^2 = 0.329$), with highest scores being reached for the identification task, followed by the discrimination task, and the olfactory threshold task (Figure 1, Table 2).

[Insert Fig. 1]

[Insert Table 2]

**Automated Odorant Identification and Localization (AOLI)**

For the sensitivity index *d'*, the rm-ANOVA yielded no significant interaction between *task* * *condition* ($F(1,20) = 0.009$, $p = 0.924$, $\eta^2 = 0.00$). There was a large main effect of *task* ($F(1,20) = 10{,}71$, $p = 0.004$, $\eta^2 = 0.349$). On average, participants performed more accurately in the identification ($M = 1.057$, $SD = 0.666$) compared to localization ($M = 0.361$, $SD = 0.856$). A significant main effect of *condition* was also observed ($F(1,20) = 5.652$, $p = 0.028$, $\eta^2 = 0.22$). Deaf individuals outperformed hearing controls in both tasks, i.e., identification and localization (Table 3).

[Insert Table 3]

On average, response bias C was slightly positive for the identification ($M = 0.253$, $SD = 0.301$) and localization ($M = 0.243$, $SD = 0.565$). No significant main effect was observed for *task* ($F(1,20) = 0.005$, $p = 0.943$, $\eta^2 = 0.00$) or *condition* ($F(1,20) = 0.421$, $p = 0.524$, $\eta^2 = 0.021$) or interaction *task* * *condition* ($F(1,20) = 0.079$, $p = 0.782$, $\eta^2 = 0.004$).

On average, response time was similar for localization ($M = 2.124$, $SD = 0.627$) and identification ($M = 2.056$, $SD = 0.686$). Again, no effect of *task* ($F(1,20) = 3.14$, $p = 0.083$, $\eta^2 = 0.015$) or interaction *task* * *condition* ($F(1,20) = 0.32$, $p = 0.860$, $\eta^2 = 0.002$) were found.

However, there was a main effect of *condition* ($F(1,20) = 6{,}001$, $p = 0.024$, $\eta^2 = 0.231$), with deaf participants ($M = 1.765$, $SD = 0.328$) being faster at accurately identifying odorants compared to hearing controls ($M = 2.346$, $SD = 0.833$). This tendency extends to the localization task: deaf individuals ($M = 1.856$, $SD = 0.436$) were significantly faster in response time than control participants ($M = 2.392$, $SD = 0.691$). Results are illustrated in Figure 2.

[Insert Fig. 2]

### Effect of Cochlear Implant

No significant difference was observed between CI users and those without CI for the Sniffin' Sticks test global score ($U = 13.5$, $p = 0.792$), AOLI identification (*d'*: $U = 9.5$, $p = 0.329$; *C*: $U = 25$, $p = 0.082$) localization (*d'*: $U = 20.5$, $p = 0.329$; *C*: $U = 18$, $p = 0.662$) or response times: identification ($U = 7$, $p = 0.117$) or localization ($U = 14$, $p = 0.931$).

## Discussion

The present study examined the impact of congenital hearing loss on several chemosensory tasks. As hypothesized, olfactory abilities and trigeminal perception are enhanced for deaf individuals compared to hearing controls in discrimination and identification tasks.

This is in line with the notion of adaptive neuroplasticity between modalities, as observed for the visual and tactile domains in previous studies (Megreya & Bindemann, 2017; Sharp et al., 2020; Simon et al., 2020; Smittenaar et al., 2016; van Dijik et al., 2013). The results are however also in contrast with some existing literature on the olfactory modality showing reduced performance for the deaf. One specific aspect may explain this difference: in contrast to earlier reports (Guducu et al., 2016; Diekmann et al., 1994), we ascertained typical cognitive function in the deaf group. In fact, only deaf individuals were included who had scores within the normative range for attention, visual memory, and fluid reasoning. This is especially important because the ability to identify and discriminate odors correlates with performance in executive function and semantic memory (e.g., Hedner et al. 2010; Larsson et al., 2000). Either altered cognitive function or a delayed language acquisition might in fact influence previous results and explain some variability (Diekmann et al., 1994), mainly for the preponderance of hyposmia and anosmia in the deaf population (Guducu et al., 2016). In fact, vocabulary knowledge is particularly important in the context of the SST identification task, as it implies a forced choice labeling of odorants (Hummel et al., 1997). Future research with individuals having limited verbal language and reading abilities therefore should use appropriate tests and adapt the means used to present the response choices (written vs signed) to ensure full comprehension of the task.

The differences with the existing literature may also partly be explained by the age of onset deafness, a factor known to influence compensatory plasticity (Lazzouni & Lepore, 2014). There is a critical period at the start of postnatal life during which the brain is most receptive to change (Oberman & Pascual-Leone, 2013). However, heterogeneity of background within the deaf sample are common limitations in the literature (Bavelier et al., 2006). In one study (Diekmann et al., 1994), only three individuals were congenitally deaf while four became profoundly deaf during the first five years. In contrast, in the present study, only participants with congenital deafness, i.e., hearing loss present at birth, were included.

Our findings therefore provide support for the notion that crossmodal sensory compensation for the auditory system extends to chemosensory domains, by showing that the sense of smell is enhanced in deaf individuals. In agreement with this hypothesis, additional contribution of neural resources to the remaining sensory streams compensate for auditory deprivation (Singh et al., 2018). Cross-modal reorganization underlies adaptive and compensatory behaviors (Merabet & Pascual-Leone, 2010). While it is accepted that sensory deprivation leads to the expansion of other senses, these compensatory effects remain complex (Kupers & Ptito, 2014). For the olfactory modality, the neurobiological underpinnings are yet to be elucidated. Future studies using functional magnetic resonance imaging (fMRI) will possibly identify the implicated brain areas associated with improved olfactory performance as the result of compensatory neuroplasticity between auditory and olfactory modalities in deafness.

The superiority of deaf individuals includes the trigeminal system, as they had superior abilities to localize odorants. In fact, the trigeminal system is a third chemosensory system next to smell and taste. The trigeminal system has a protective function, which is reflected in various physiological reflexes such as salivation, tearing, coughing, respiratory depression, and sneezing (Viana, 2011). Its sensitivity can be assessed with the odor localization task used in the present study and validated by past ones (Frasnelli et al., 2007). This observation is also in line with results on individuals with early blindness (Manescu et al., 2021).

In addition to better response sensitivity, the results of this study also indicate that deaf individuals responded faster on the localization and identification tasks, the latter correlating with response accuracy (Kéïta et al., 2013). There is evidence that sensory deprivation affects the visual function, especially spatial information presented at the periphery, resulting in faster reaction time to stimuli (Bottari et al., 2011; Chen et al., 2006; Codina et al., 2017; Nava et al., 2008; Prasad et al., 2017). This advantage appears to emerge in adolescence and transfer to adulthood (Codina et al., 2011). It is possible that response time in olfactory function constitutes a behavioral compensation for deafness-induced neuroplasticity, similar to what is found in the visual modality.

One possible shortcoming of our study is the fact that five of the eleven deaf individuals were implanted with a CIs at the time of testing. Three of them were implanted before the age of

3.5, meaning that they had access to some form of auditory input during the sensitive period when the central auditory system is most receptive to change (Sharma et al., 2002). To ascertain that this was not a confounding factor, the five CI users were compared with the rest of the deaf sample and no statistically significant differences were found. However, in future studies, CI users will be treated as a separate group, as there are implications for the means of communication (oral or signed) and the degree of neuroplasticity. Larger sample sizes would allow to draw stronger conclusions about the use of CI and age of implantation on olfactory/trigeminal functions, as much as to confirm the present findings. It is to be noted that the handedness of participants is only available for controls, all of whom were right-handed.

## Conclusion

Psychophysical olfactory assessment methods were used to evaluate the influence of congenital hearing loss on chemosensory systems. Compared to controls, individuals with severe-to-profound congenital deafness but typical cognition had significantly higher olfactory scores. In addition, they were more sensitive to trigeminal odor localization.

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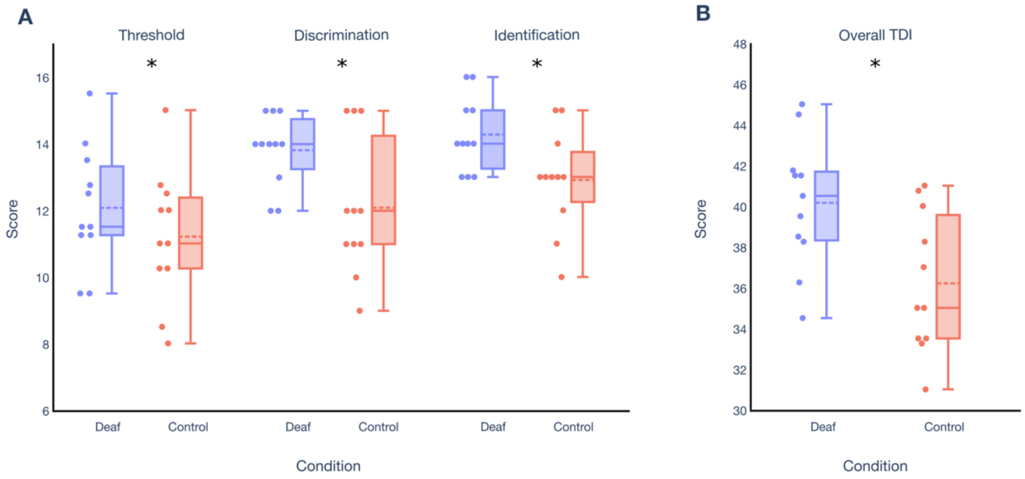
**Figure 1**

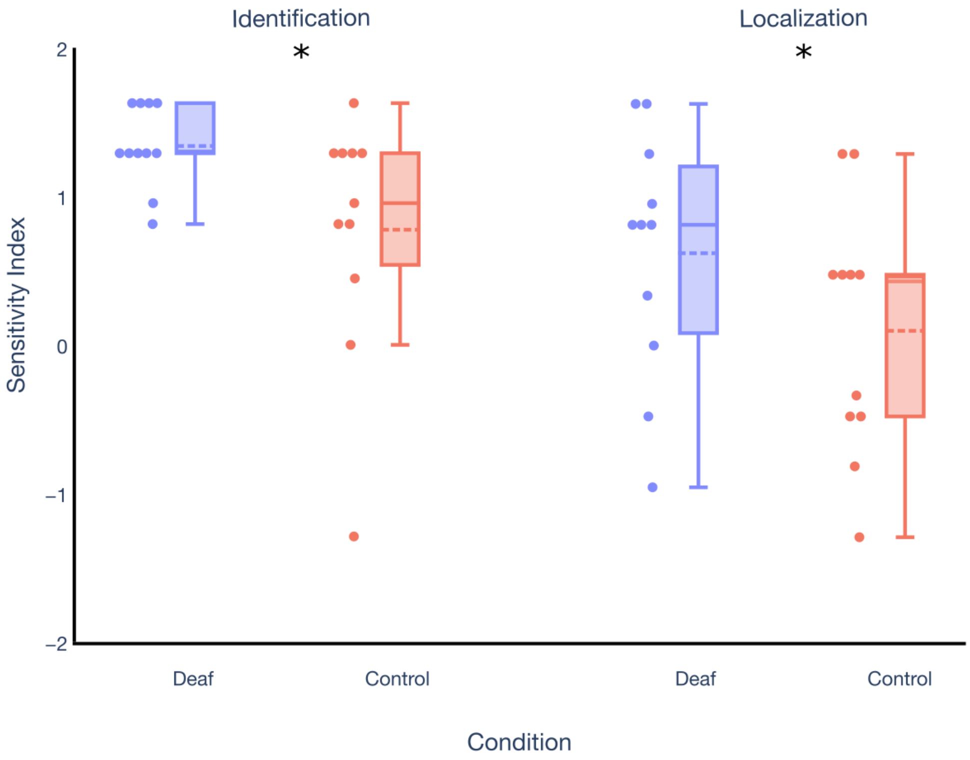
*Mean scores Distribution on the Sniffin' Sticks Test, Separated by Condition (Deaf, Control) and Tasks (Olfactory Threshold, Discrimination, Identification) and Overall TDI*



*Note*. $^A$Olfactory detection threshold, discrimination, and identification scores, each out of 16 and $^B$Overall TDI, score out of 48. Asterisk indicates a significant group effect at $p < 0.05$. The dashed line in the box represents the mean value, while the solid line represents the median. The first and third quartile are delimited by the lower and upper horizontal line of the boxplot. The minimum and maximum values are indicated by the lower and upper fences, respectively. Each point designates the performance of one participant.

**Figure 2**

*Sensitivity Index d' Separated by Condition (Deaf, Control) and Task (Odor Identification, Odor Localization)*



*Note*. Asterisk indicates a significant group effect at $p < 0.05$. The dashed line in the box represents the mean value, while the solid line represents the median. The first and third quartile are delimited by the lower and upper horizontal line of the boxplot. The minimum and maximum values are indicated by the lower and upper fences, respectively. Each point designates the performance of one participant.

**Table 1**

*Descriptive Characteristics of Participants*

| Id | Condition | Age (years) | Gender | Education (years) | Language preference | CI duration (years) |
|---|---|---|---|---|---|---|
| 1 | D | 45 | F | 16 | LSQ + French | 42 |
| 2 | D | 28 | F | 14 | LSQ + French | 24 |
| 3 | D | 20 | M | 14 | LSQ + French | 18 |
| 4 | D | 28 | M | 16 | French | 27 |
| 5 | D | 47 | M | 9 | French | 42 |
| 6 | D | 51 | F | 7 | LSQ | N/A |
| 7 | D | 36 | F | 16 | LSQ | N/A |
| 8 | D | 32 | F | 14 | LSQ | N/A |
| 9 | D | 35 | M | 16 | LSQ | N/A |
| 10 | D | 28 | F | 16 | LSQ | N/A |
| 11 | D | 42 | F | 11 | LSQ | N/A |
| 12 | H | 46 | F | 11 | French | N/A |
| 13 | H | 47 | M | 16 | French | N/A |
| 14 | H | 52 | F | 13 | French | N/A |
| 15 | H | 36 | F | 16 | French | N/A |
| 16 | H | 31 | F | 16 | French | N/A |
| 17 | H | 20 | M | 14 | French | N/A |
| 18 | H | 34 | M | 14 | French | N/A |
| 19 | H | 28 | M | 16 | French | N/A |
| 20 | H | 27 | F | 21 | French | N/A |
| 21 | H | 26 | F | 18 | French | N/A |
| 22 | H | 45 | F | 12 | French | N/A |

*Note*. D = Deaf individuals; H = Hearing individuals; F = female; M = male; LSQ = Quebec Sign Language; CI = Cochlear implant; N/A = Not applicable.

**Table 2**

*Sniffin' Sticks Test Descriptive Statistics Separated by Task (Threshold, Discrimination, Identification) and Condition (Deaf, Control)*

| | Threshold | | Discrimination | | Identification | |
|---|---|---|---|---|---|---|
| | Deaf | Control | Deaf | Control | Deaf | Control |
| *N* | 11 | 11 | 11 | 11 | 11 | 11 |
| *Mean* | 12.068 | 11.205 | 13.818 | 12.091 | 14.273 | 12.909 |
| *SD* | 1.827 | 1.981 | 1.079 | 2.071 | 1.104 | 1.514 |
| *SE* | 0.575 | 0.575 | 0.498 | 0.498 | 0.399 | 0.399 |
| *Lower limit* | 10.87 | 10.006 | 12.780 | 11.052 | 13.440 | 12.076 |
| *Upper limit* | 13.267 | 12.403 | 14.857 | 13.130 | 15.106 | 13.742 |
| *P* | | | 0.011 | | | |

**Table 3**

*Automated Identification and Localization Descriptive Statistics Separated by Measure (Sensitivity Index, Response Bias) and Condition (Deaf, Control)*

| | Identification | | | | Localization | | | |
|---|---|---|---|---|---|---|---|---|
| | Sensitivity index | | Response bias | | Sensitivity index | | Response bias | |
| | Deaf | Control | Deaf | Control | Deaf | Control | Deaf | Control |
| *N* | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 |
| *Mean* | 1.339 | 0.775 | 0.227 | 0.280 | 0.622 | 0.100 | 0.178 | 0.309 |
| *SD* | 0.277 | 0.824 | 0.257 | 0.350 | 0.827 | 0.838 | 0.603 | 0.546 |
| *SE* | 0.185 | 0.185 | 0.093 | 0.093 | 0.251 | 0.251 | 0.173 | 0.173 |
| *Lower limit* | 0.952 | 0.388 | 0.034 | 0.087 | 0.98 | -0.424 | -0.183 | -0.053 |
| *Upper limit* | 1.725 | 1.162 | 0.420 | 0.473 | 1.146 | 0.623 | 0.540 | 0.670 |
| *P* | | | | 0.028 | | | | |